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SEARCH REQUEST FORM

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Requester's Full Name: Mansfield Examiner #: 71976 Date: 7/15/02
Art Unit: 1645 Phone Number 30 5 3394 Serial Number: 09/955739
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If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Urease-based Vaccine + Treatment for Helicobacter Infect

Inventors (please provide full names): Pierre Michetti, Irene Corthesy-Theulaz, Andre Blum, Catherine Davin, Rainer Haas, Jean-Pierre Kraehenbuhl, Emilia Saraga

Earliest Priority Filing Date: 2/23/94

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Method to treat gastroduodenal disease, administer Helicobacter urease peptides.
urease B peptide

Search diseases include: Gastritis, peptic ulcer disease chronic dyspepsia, severe erosive gastroduodenitis, refactory non-ulcer dyspepsia, intestinal metaplasia low grade MALT lymphoma, Helicobacter infection, Helicobacter pylori infection, H. felis disease

urease, urease B, Helicobacter urease
H. pylori urease

Search author/inventor names

Thanks
Mansfield

****

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Searcher: M Smith
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Searcher Location:
Date Searcher Picked Up: 07/16/02
Date Completed: 07/23/02
Searcher Prep & Review Time: 65
Clerical Prep Time:
Online Time: 70

Type of Search

NA Sequence (#)
AA Sequence (#)
Structure (#)
Bibliographic X
Litigation
Fulltext
Patent Family
Other

Vendors and cost where applicable

STN
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Questel/Orbit
Dr.Link
Lexis/Nexis
Sequence Systems
WWW/Internet
Other (specify)

PTO-1590 (8-01)

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FILE LAST UPDATED: 21 Jul 2002  (20020721/ED)

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L1           30 SEA FILE=HCAPLUS ((MICHETTI P?) OR (MICHETTI,P?) OR (MICHETTI,
                P?))/AU,IN
L2          540 SEA FILE=HCAPLUS ((BLUM A?) OR (BLUM,A?) OR (BLUM, A?))/AU,IN
L3            6 SEA FILE=HCAPLUS ((DAVIN C?) OR (DAVIN,C?) OR (DAVIN, C?))/AU,I
                N
L4          651 SEA FILE=HCAPLUS ((HAAS R?) OR (HAAS,R?) OR (HAAS, R?))/AU,IN
L5          169 SEA FILE=HCAPLUS ("KRAEHENBUHL J P"/AU OR "KRAEHENBUHL JEAN
                P"/AU OR "KRAEHENBUHL JEAN PIERRE"/AU OR "KRAEHENBUHL JEAN
                PIERRE"/IN)
L6           18 SEA FILE=HCAPLUS ("SARAGA E"/AU OR "SARAGA EMILIA"/AU OR
                "SARAGA EMILIA"/IN OR "SARAGA EMILIA P"/AU)
L7           31 SEA FILE=HCAPLUS "CORTHESY IRENE"/AU OR ("CORTHESY THEULAZ
                I"/AU OR "CORTHESY THEULAZ I E"/AU OR "CORTHESY THEULAZ
                IRENE"/AU OR "CORTHESY THEULAZ IRENE"/IN OR "CORTHESY THEULAZ
                IRENE E"/AU)
L8         1381 SEA FILE=HCAPLUS L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7
L9          119 SEA FILE=HCAPLUS L8 AND (GASTR? OR ULCER?)
L10          36 SEA FILE=HCAPLUS L9 AND HELICOBACT?


=> d ibib abs hitrn l10 1-36

L10  ANSWER 1 OF 36  HCAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2002:489737  HCAPLUS
TITLE:                    Essential role of ferritin Pfr in Helicobacter
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pylori iron metabolism and **gastric** colonization

AUTHOR(S): Waidner, Barbara; Greiner, Stefan; Odenbreit, Stefan; Kavermann, Holger; Velayudhan, Jyoti; Stahler, Frank; Guhl, Johannes; Bisse, Emmanuel; Van Vliet, Arnoud H. M.; Andrews, Simon C.; Kusters, Johannes G.; Kelly, David J.; **Haas, Rainer**; Kist, Manfred; Bereswill, Stefan

CORPORATE SOURCE: Institute of Medical Microbiology and Hygiene, Department of Medical Microbiology and Hygiene, University Hospital of Freiburg, Freiburg, D-79104, Germany

SOURCE: Infection and Immunity (2002), 70(7), 3923-3929
CODEN: INFIBR; ISSN: 0019-9567

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The reactivity of the essential element iron necessitates a concerted expression of ferritins, which mediate iron storage in a nonreactive state. Here we have further established the role of the **Helicobacter** pylori ferritin Pfr in iron metab. and **gastric** colonization. Iron stored in Pfr enabled H. pylori to multiply under severe iron starvation and protected the bacteria from acid-amplified iron toxicity, as inactivation of the pfr gene restricted growth of H. pylori under these conditions. The lowered total iron content in the pfr mutant, which is probably caused by decreased iron uptake rates, was also reflected by an increased resistance to superoxide stress. Iron induction of Pfr synthesis was clearly diminished in an H. pylori feoB mutant, which lacked high-affinity ferrous iron transport, confirming that Pfr expression is mediated by changes in the cytoplasmic iron pool and not by extracellular iron. This is well in agreement with the recent discovery that iron induces Pfr synthesis by abolishing Fur-mediated repression of pfr transcription, which was further confirmed here by the observation that iron inhibited the in vitro binding of recombinant H. pylori Fur to the pfr promoter region. The functions of H. pylori Pfr in iron metab. are essential for survival in the **gastric** mucosa, as the pfr mutant was unable to colonize in a Mongolian gerbil-based animal model. In summary, the pfr phenotypes obsd. give new insights into prokaryotic ferritin functions and indicate that iron storage and homeostasis are of extraordinary importance for H. pylori to survive in its hostile natural environment.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2002:225421 HCAPLUS

DOCUMENT NUMBER: 136:351799

TITLE: Activation of **Helicobacter** pylori CagA by tyrosine phosphorylation is essential for dephosphorylation of host cell proteins in **gastric** epithelial cells

AUTHOR(S): Puls, Jurgen; Fischer, Wolfgang; **Haas, Rainer**

CORPORATE SOURCE: Max von Pettenkofer Institut fur Hygiene und Medizinische Mikrobiologie, LMU Munchen, Munchen,

D-80336, Germany
SOURCE: Molecular Microbiology (2002), 43(4), 961-969
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Helicobacter** pylori type I strains harbor the cag pathogenicity island (cag-PAI), a 37 kb sequence, which encodes the components of a type IV secretion system. CagA, the first identified effector protein of the cag-PAI, is translocated into eukaryotic cells and tyrosine phosphorylated (CagAP-tyr) by a host cell tyrosine kinase. Translocation of CagA induces the dephosphorylation of a set of phosphorylated host cell proteins of unknown identity. CagA proteins of independent H. pylori strains vary in sequence and thus in the no. and compn. of putative tyrosine phosphorylation motifs (TPMs). The CagA protein of H. pylori strain J99 (CagAJ99) does not carry any of three putative tyrosine phosphorylation motifs (TPM-A, TPM-B or TPM-C) predicted by the MOTIF algorithm in CagA proteins. CagAJ99 is not tyrosine phosphorylated and is inactive in the dephosphorylation of host cell proteins. By site-specific mutagenesis, we introduced a TPM-C into CagAJ99 by replacing a single lysine with a tyrosine. This slight modification resulted in tyrosine phosphorylation of CagAJ99 and host cell protein dephosphorylation. In contrast, the removal of the indigenous TPM-C from CagAP12 did not abolish its tyrosine phosphorylation, suggesting that further phosphorylated sites are present in CagAP12. By generation of hybrid CagA proteins, a phosphorylation of the most N-terminal TPM-A could be excluded. Our data suggest that tyrosine phosphorylation at TPM-C is sufficient, but not exclusive, to activate translocated CagA. Activated CagAP-tyr might either convert into a phosphatase itself or activate a cellular phosphatase to dephosphorylate cellular phosphoproteins and modulate cellular signaling cascades of the host.
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:584680 HCAPLUS
DOCUMENT NUMBER: 136:196821
TITLE: Natural transformation competence in **Helicobacter** pylori is mediated by the basic components of a type IV secretion system
AUTHOR(S): Hofreuter, Dirk; Odenbreit, Stefan; **Haas, Rainer**
CORPORATE SOURCE: Max von Pettenkofer Institut fur Hygiene und Medizinische Mikrobiologie, Munchen, D-80336, Germany
SOURCE: Molecular Microbiology (2001), 41(2), 379-391
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Helicobacter** pylori (Hp), a Gram-neg. bacterial pathogen and etiol. agent of **gastroduodenal** disease in humans, is naturally competent for genetic transformation. Natural competence in bacteria is usually correlated with the presence of type IV pili or type IV pilin-like proteins, which are absent in Hp. Instead, we recently identified the

comB operon in Hp, carrying four genes tentatively designated as orf2, comB1, comB2 and comB3. We show here that all ComB proteins and the 37-amino-acid Orf2 peptide display significant primary sequence and structural homol./identity to the basic components of a type IV secretion app. ComB1, ComB2 and ComB3, now renamed ComB8, ComB9 and ComB10, correspond to the Agrobacterium tumefaciens VirB8, VirB9 and VirB10 proteins resp. The peptide Orf2 carries a lipoprotein motif and a second cysteine residue homologous to VirB7, and was thus designated ComB7. The putative ATPase ComB4, encoded by the open reading frame hp0017 of strain 26695, corresponds to virB4 of the A. tumefaciens type IV secretion system. A Hp comB4 transposon insertion mutant was totally defective in natural transformation. By complementation of a Hp .DELTA.comB deletion mutant, we demonstrate that each of the proteins from ComB8 to ComB10 is absolutely essential for the development of natural transformation competence. The putative lipoprotein ComB7 is not essential, but apparently stabilizes the app. and modulates the transformation efficiency. Thus, pathogenic type I Hp strains contain two functional independent type IV transport systems, one for protein translocation encoded by the cag pathogenicity island and one for uptake of DNA by natural transformation. The latter system indicates a possible novel mechanism for natural DNA transformation in bacteria.

REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:305032 HCAPLUS
DOCUMENT NUMBER: 135:225368
TITLE: Development of a **Helicobacter** pylori vaccine
AUTHOR(S): Banerjee, Subhas; **Michetti, Pierre**
CORPORATE SOURCE: Div. Gastroenterol., Beth Iserael Deaconess med. Cent., Harvard Med. Sch., Boston, MA, USA
SOURCE: Helicobacter pylori (2001), 263-274. Editor(s): Achtman, Mark; Suerbaum, Sebastian. Horizon Scientific Press: Wymondham, UK.
CODEN: 69AYWT
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English

AB A review with 67 refs. Novel strategies are needed to control H. pylori infection on a global scale and the potential value of a vaccine is increasingly recognized. Studies in rodents have demonstrated the feasibility of prophylactic and therapeutic mucosal immunization against **Helicobacter** infections. Initial human trials showed that oral immunization with H. pylori urease is safe, immunogenic, and can result in a decreased **gastric** bacterial load. However, more potent vaccines will be needed to protect against or cure H. pylori infection in humans. To achieve this goal, our knowledge of the mechanisms of immune protection in the stomach needs to be improved. In rodents, the MHC II-restricted CD4+ T cell response plays a prominent role whereas antibodies are not necessary for protection. In humans, mechanisms that mediate protection against noninvasive **gastric** pathogens are largely unknown. Multivalent vaccines, safe adjuvants, and improved vaccine delivery systems all need to be studied. Divalent combinations of antigens are superior to single antigen vaccines in rodents. The availability of two genomic sequences of H. pylori will certainly help

identify addnl. candidate vaccine antigens. Detoxified bacterial toxin adjuvants, live vaccine vectors and alternate routes of immunization are currently being actively evaluated.

REFERENCE COUNT: 67 THERE ARE 67 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:116230 HCAPLUS
DOCUMENT NUMBER: 135:146510
TITLE: **Helicobacter** pylori, an adherent pain in the stomach
AUTHOR(S): Gerhard, Markus; Hirmo, Siiri; Wadstrom, Torkel; Miller-Podraza, Halina; Teneberg, Susann; Karlsson, Karl-Anders; Appelmelk, Ben; Odenbreit, Stefan; **Haas, Rainer**; Arnqvist, Anna; Boren, Thomas
CORPORATE SOURCE: Department of Medicine II, Technical University of Munich, Munich, 81675, Germany
SOURCE: Helicobacter pylori (2001), 185-206. Editor(s): Achtman, Mark; Suerbaum, Sebastian. Horizon Scientific Press: Wymondham, UK.
CODEN: 69AYWT
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with many refs. Modern strains of **Helicobacter** pylori are the result of selection for life in the human **gastric** mucosa. This is a most demanding environment, with high acidity, peristalsis, **gastric** emptying and shedding of cells and mucus. In order to ensure efficient long-term survival and colonization, these microbes have developed arrays of adherence properties for homing to the optimal set of host cells. Survival demands an adequate balance between movement due to flagellar motility and attachment by adherence. This balance allows the microbes to take advantage of continuous supplies of nutrients without cutting off escape from the mucus layer to evade the cellular immune responses. H. pylori possesses a multitude of genetic mechanisms for the flexible shifting of adherence specificities to allow adaptation to the host and the local environment. The detailed characterization of the mechanisms that support and maintain bacterial adherence will identify key-elements for the persistence of infection that can be targeted for anti-microbial drug strategies.

L10 ANSWER 6 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:95344 HCAPLUS
DOCUMENT NUMBER: 134:263292
TITLE: Interaction of **Helicobacter** pylori with professional phagocytes: role of the cag pathogenicity island and translocation, phosphorylation and processing of CagA
AUTHOR(S): Odenbreit, Stefan; Gebert, Bettina; Puls, Jurgen; Fischer, Wolfgang; **Haas, Rainer**
CORPORATE SOURCE: Max von Pettenkofer Institut fur Hygiene und Medizinische Mikrobiologie, Munchen, D-80336, Germany
SOURCE: Cellular Microbiology (2001), 3(1), 21-31
CODEN: CEMIF5; ISSN: 1462-5814
PUBLISHER: Blackwell Science Ltd.

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Chronic infection of the human **gastric** mucosa with **Helicobacter** pylori is a major cause of **gastroduodenal** pathologies, including peptic **ulcerations**, mucosa-assocd. lymphoid tissue (MALT) lymphoma and adenocarcinoma. **Helicobacter** pylori strains carrying the cag pathogenicity island, which encodes an active type IV protein secretion system (cag+ or type I strains), are preferentially assocd. with strong **gastric** inflammation and severe disease. We show here that cag+ H. pylori strains use the type IV secretion system to inject the bacterial protein CagA into various types of professional phagocytes, including human polymorphonuclear leukocytes (PMNs) and the human and murine macrophage cell lines THP-1 and J774A.1. CagA is rapidly tyrosine phosphorylated and proteolytically processed to generate a stable 35-45 kDa C-terminally tyrosine-phosphorylated protein fragment. H. pylori was efficiently ingested by the different types of phagocytic cells. A chromosomal deletion of the complete pathogenicity island had no significant effect on the rate of ingestion. Furthermore, the survival rate of H. pylori in the phagosome was unchanged between the wild type and a deletion mutant lacking the type IV secretion system. Thus, the type IV secretion system seems to be involved neither in active phagocytosis resistance nor in prolonged survival of the bacteria in phagocytic cells.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:555659 HCAPLUS
DOCUMENT NUMBER: 134:130191
TITLE: **Gastric** mucosal .alpha.4.beta.7-integrin-positive CD4 T lymphocytes and immune protection against **Helicobacter** infection in mice
AUTHOR(S): Michetti, Murielle; Kelly, Ciaran P.; **Kraehenbuhl**, **Jean-Pierre**; Bouzourene, Hanifa; **Michetti**, **Pierre**
CORPORATE SOURCE: Division of Gastroenterology, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA, USA
SOURCE: Gastroenterology (2000), 119(1), 109-118
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The integrin .alpha.4.beta.7 mediates homing of effector/memory lymphocytes to the intestine and the mucosa-assocd. lymphoid tissue. This study examd. the ability of .alpha.4.beta.7hi CD4+ T lymphocytes to home to the stomach and their role in immunization-mediated protection against **Helicobacter** felis infection. **Gastric** lamina propria and circulating mononucleated cells of naive, infected, and immunized Swiss Webster mice were isolated, and .alpha.4.beta.7-integrin expression was quantified by flow cytometry on CD4+ T lymphocytes. Anti-.alpha.4.beta.7-integrin antibody was used to block .alpha.4.beta.7 function in vivo. In naive mice, .alpha.4.beta.7hi CD4+ T cells were enriched approx. 10-fold in the **gastric** mucosa compared with

peripheral blood. Chronic H. felis infection did not alter these proportions, but oral immunization with H. felis sonicate plus cholera toxin (CT) or with CT alone markedly increased **gastric** .alpha.4.beta.7hi CD4+ T cells compared with naive and infected controls. Anti-.alpha.4.beta.7-integrin antibody blocked the protection induced by oral immunization with H. felis sonicate and CT. The integrin .alpha.4.beta.7 participates in the homing of CD4+ T lymphocytes to the stomach and in the protection of the **gastric** mucosa against H. felis infection.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:340294 HCAPLUS
DOCUMENT NUMBER: 134:111039
TITLE: Rapid and specific detection of **Helicobacter** pylori macrolide resistance in **gastric** tissue by fluorescent in situ hybridisation
AUTHOR(S): Trebesius, K.; Panthel, K.; Strobel, S.; Vogt, K.; Faller, G.; Kirchner, T.; Kist, M.; Heesemann, J.; **Haas, R.**
CORPORATE SOURCE: Max von Pettenkofer Institute for Hygiene and Medical Microbiology, Ludwig Maximilians, University Munich, Germany
SOURCE: Gut (2000), 46(5), 608-614
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background-The development of macrolide resistance in **Helicobacter** pylori is considered an essential reason for failure of antibiotic eradication therapies. The predominant mechanism of resistance to macrolides, particularly clarithromycin, is based on three defined mutations within 23S rRNA, resulting in decreased binding of the antibiotic to the bacterial ribosome. Aim-To develop an rRNA based whole cell hybridization method to detect **Helicobacter** species in situ within **gastric** tissue, simultaneously with its clarithromycin resistance genotype. Methods-A set of fluorescent labeled oligonucleotide probes was developed, binding either to H pylori 16S rRNA or 23S rRNA sequences contg. specific point mutations responsible for clarithromycin resistance. After hybridization and stringent washing procedures, labeling of intact single bacteria was monitored by fluorescence microscopy. The new approach was compared with PCR based assays, histol., and microbiol. culture. Results-In comparison with the phenotypic resistance measurement by E test, the genotypic clarithromycin resistance correlated perfectly (100%) for 35 H pylori isolates analyzed. In a set of **gastric** biopsy specimens (27) H pylori infection was confirmed by histol. (17/27) and correctly detected by whole cell hybridization. Five clarithromycin resistant strains were identified in **gastric** tissue specimens directly. Furthermore, non-cultivable coccoid forms of H pylori were easily detectable by whole cell hybridization. Conclusions-Whole cell hybridization of rRNA holds great promise for cultivation independent, reliable, and rapid (three hours) genotypic detn. of clarithromycin resistance in H pylori. Compared with

PCR techniques it is independent of nucleic acid prepns., not prone to inhibition, and allows semiquant. visualisation of the bacteria within intact tissue samples.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:291921 HCAPLUS
DOCUMENT NUMBER: 132:288595
TITLE: The effect of ammonia on omeprazole-induced reduction of **gastric** acidity in subjects with **Helicobacter** pylori infection
AUTHOR(S): Bercik, Premysl; Verdu, Elena F.; Armstrong, David; Idstrom, Jan-Peter; Cederberg, Christer; Markert, Michele; Crabtree, Jean E.; Stolte, Manfred; **Blum, Andre L.**
CORPORATE SOURCE: Division of Gastroenterology and Central Laboratory of Clinical Chemistry, CHUV, Lausanne, Switz.
SOURCE: American Journal of Gastroenterology (2000), 95(4), 947-955
CODEN: AJGAAR; ISSN: 0002-9270
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Omeprazole produces a higher intragastric pH during **Helicobacter** pylori (H. pylori) infection than after cure. We tested the hypothesis that this difference is due to the prodn. of ammonia by H. pylori. **Gastric** acidity and acid output (AO) were measured overnight in 12 subjects, with and without omeprazole, before and 1 and 6 mo after cure of H. pylori infection. **Gastric** ammonia ([NH3]), total bile acid ([TBA]) and protein concns. and plasma omeprazole levels were measured. During omeprazole, median AO were 0.0 mmol/h before, 0.86 mmol/h ($p = 0.003$ vs before cure) at 1 mo, and 0.34 mmol/h ($p = 0.02$) at 6 mo after cure; median NH3 output was 0.17 mmol/h before, 0.03 mmol/h ($p = 0.002$) at 1 mo, and 0.02 mmol/h ($p = 0.005$) at 6 mo after cure. AO and NH3 output were similar 1 and 6 mo after cure. When cor. for [NH3], AO and **gastric** pH curves were similar before and after cure. Omeprazole plasma levels increased after cure and **gastric** [TBA] were unchanged. The higher pH obsd. before cure of H. pylori during omeprazole administration is attributable, in large part, to ammonia prodn. Other acid-neutralizing substances and changes in acid secretion may also be important, but duodenogastric reflex and omeprazole pharmacokinetics are not involved.
REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:228868 HCAPLUS
DOCUMENT NUMBER: 133:131032
TITLE: The effect of intra-**gastric** acidity and flora on the concentration of N-nitroso compounds in the stomach
AUTHOR(S): Viani, Francesco; Siegrist, Hans H.; Pignatelli, Brigitte; Cederberg, Christer; Idstrom, Jan-Peter;

Verdu, Elena F.; Fried, Michael; **Blum, Andre L.**; Armstrong, David
CORPORATE SOURCE: Department of Gastroenterology, University Hospital, Lausanne, Switz.
SOURCE: European Journal of Gastroenterology & Hepatology (2000), 12(2), 165-173
CODEN: EJGHES; ISSN: 0954-691X
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Correa's hypothesis proposes that **gastric** carcinogenesis is due to atrophic **gastritis** and hypochlorhydria which permit **gastric** bacterial colonization, the redn. of dietary nitrates to nitrites and the formation of potentially carcinogenic N-nitroso compds. (NOCs). To test the hypothesis that omeprazole-induced hypochlorhydria is assocd. with increased intra-**gastric** concns. of nitrate-reducing bacteria (NRB), nitrites and NOCs, a single-blind study was conducted in healthy volunteers. The participants were 14 healthy subjects (seven female, mean age 24 yr), free of **Helicobacter** pylori infection, who received a one-week course of placebo followed by a two-week course of omeprazole, 20 mg daily. Fasted **gastric** samples, aspirated using a sterile double-lumen nasogastric tube at the end of the 1st week (placebo) and the 2nd and 3rd weeks (omeprazole), were cultured aerobically and anaerobically; **gastric** pH and intra-**gastric** concns. of nitrates, nitrites and NOCs were also detd. After weeks 1, 2 and 3, the intra-**gastric** concns. of nitrate-reducing bacteria exceeded 105 colony-forming units (c.f.u.)/mL in 3, 7 and 9 subjects, resp. A **gastric** pH >4.0 was assocd. with increased NRB; however, neither increased **gastric** pH nor increased NRB, alone or in combination, was assocd. with increased intra-**gastric** concns. of nitrites or NOCs. A two-week increase in **gastric** pH in healthy, H. pylori-neg. subjects was assocd. with increased intra-**gastric** concns. of nitrate-reducing bacteria but not of nitrites or N-nitroso compds. These data suggest that reduced **gastric** acid secretion is not a necessary precursor to the formation of carcinogenic N-nitroso compds. and that other mechanisms should be invoked to explain **gastric** carcinogenesis.
REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:149963 HCAPLUS
DOCUMENT NUMBER: 132:277466
TITLE: Translocation of **Helicobacter** pylori CagA into **gastric** epithelial cells by type IV secretion
AUTHOR(S): Odenbreit, Stefan; Pills, Jurgen; Sedimaier, Bettina; Gerland, Elke; Fischer, Wolfgang; **Haas, Rainer**
CORPORATE SOURCE: Max von Pettenkofer Inst. Hygiene and Med. Microbiology, Ludwig-Maximilians Univ. Munich, Munich, D-80336, Germany
SOURCE: Science (Washington, D. C.) (2000), 287(5457), 1497-1500
CODEN: SCIEAS; ISSN: 0036-8075

PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The Gram-neg. bacterium **Helicobacter** pylori is a causative agent of **gastritis** and peptic **ulcer** disease in humans. Strains producing the CagA antigen (cagA+) induce strong **gastric** inflammation and are strongly assocd. with **gastric** adenocarcinoma and MALT Lymphoma. We show here that such strains translocate the bacterial protein CagA into **gastric** epithelial cells by a type IV secretion system, encoded by the cag pathogenicity island. CagA is tyrosine-phosphorylated and induces changes in the tyrosine phosphorylation state of distinct cellular proteins. Modulation of host cells by bacterial protein translocation adds a new dimension to the chronic **Helicobacter** infection with yet unknown consequences.

L10 ANSWER 12 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:108369 HCAPLUS
DOCUMENT NUMBER: 132:249351
TITLE: **Helicobacter** pylori activates the histidine decarboxylase promoter through a mitogen-activated protein kinase pathway independent of pathogenicity island-encoded virulence factors
AUTHOR(S): Wessler, Silja; Hocker, Michael; Fischer, Wolfgang; Wang, Timothy C.; Rosewicz, Stefan; **Haas, Rainer**; Wiedenmann, Bertram; Meyer, Thomas F.; Naumann, Michael
CORPORATE SOURCE: Max-Planck-Institut fur Infektionsbiologie, Abteilung Molekulare Biologie, Berlin, Germany
SOURCE: Journal of Biological Chemistry (2000), 275(5), 3629-3636
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Helicobacter** pylori infection of the **gastric** mucosa is accompanied by an activated histamine metab. Histamine plays a central role in the regulation of **gastric** acid secretion and is involved in the pathogenesis of **gastroduodenal ulcerations**. Histidine decarboxylase (HDC) is the rate-limiting enzyme for histamine prodn., and its activity is regulated through transcriptional mechanisms. The present study investigated the effect of H. pylori infection on the transcriptional activity of the human HDC (hHDC) promoter in a **gastric** epithelial cell line (AGS) and analyzed the underlying mol. mechanisms. Our studies demonstrate that H. pylori infection potently transactivated the hHDC promoter. The H. pylori-responsive element of the hHDC gene was mapped to the sequence +1 to +27 base pairs, which shows no homol. to known cis-acting elements and also functions as a **gastrin**-responsive element. H. pylori regulates the activity of this element via a Raf-1/MEK/ERK pathway, which was activated in a Ras-independent manner. Furthermore, we found that H. pylori-induced transactivation of the hHDC promoter was independent of the cag pathogenicity island and the vacuolating cytotoxin A gene and therefore

may be exerted through (a) new virulence factor(s). A better understanding of H. pylori-directed hHDC transcription can provide novel insights into the mol. mechanisms of H. pylori-dependent gene regulation in **gastric** epithelial cells and may lead to new therapeutic approaches.

REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:764237 HCAPLUS
DOCUMENT NUMBER: 132:20800
TITLE: Determination of antibiotic resistance of microorganisms by in situ hybridization using mutation-specific 23S rRNA-targetted oligonucleotide probes
INVENTOR(S): **Haas, Rainer**; Trebesius, Karlheinz; Apfel, Heiko
PATENT ASSIGNEE(S): Creatogen Biosciences G.m.b.H., Germany
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9961660	A1	19991202	WO 1999-EP3527	19990521
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19916610	A1	19991125	DE 1999-19916610	19990413
CA 2329057	AA	19991202	CA 1999-2329057	19990521
AU 9942658	A1	19991213	AU 1999-42658	19990521
BR 9910646	A	20010130	BR 1999-10646	19990521
EP 1078104	A1	20010228	EP 1999-938039	19990521
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE, IE				
JP 2002516665	T2	20020611	JP 2000-551040	19990521

PRIORITY APPLN. INFO.: DE 1998-19823098 A 19980522
DE 1999-19916610 A 19990413
WO 1999-EP3527 W 19990521

AB The invention concerns the detn. of bacterial antibiotic resistance by in situ hybridization using a combination of at least two mutation-specific 23S rRNA-targetted oligonucleotide probes, along with probes that are targetted to E.coli homologous regions of Heliobacter pylori 16S rRNA. Probes are fluorescent or enzyme labeled; samples are tissues or body fluids; microorganisms are isolated; detected without culturing or cultured; cell walls are made permeable; and nucleic acids are isolated

for in situ hybridization. Fluorescence microscopy is used for detection. **Helicobacter** species, Mycobacteria, Chlamydia, etc. can be identified and the antibiotic resistance detd. by the method. Resistance to macrolides, lincosamide, aminoglycosides, aminocyclitol, tetracycline and chloramphenicol can be detected. The invention also concerns a test kit contg. the necessary reagents and probes.

REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:717013 HCAPLUS
DOCUMENT NUMBER: 132:48418
TITLE: Activation of activator protein 1 and stress response kinases in epithelial cells colonized by **Helicobacter** pylori encoding the cag pathogenicity island
AUTHOR(S): Naumann, Michael; Wessler, Silja; Bartsch, Cornelia; Wieland, Bjorn; Covacci, Antonello; **Haas, Rainer**; Meyer, Thomas F.
CORPORATE SOURCE: Max-Planck-Institut fur Infektionsbiologie, Abteilung Molekulare Biologie, Berlin, 10117, Germany
SOURCE: Journal of Biological Chemistry (1999), 274(44), 31655-31662
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Helicobacter** pylori interacts with the apical membrane of the **gastric** epithelium and induces a no. of proinflammatory cytokines/chemokines. The subsequent infiltration of macrophages and granulocytes into the mucosa leads to **gastric** inflammation accompanied by epithelial degeneration. **Gastric** diseases, e.g. peptic **ulcer** or **gastric** adenocarcinoma, are more common among people infected with H. pylori strains producing VacA (vacuolating cytotoxin A) and possessing a cag (cytotoxin-assocd. antigen A) pathogenicity island. For the induction of the cytokine/chemokine genes in response to H. pylori, we studied the signaling leading to the nuclear activation of the early response transcription factor activator protein 1 (AP-1). We found that H. pylori strains carrying the pathogenicity island induce activation of AP-1 and nuclear factor .kappa.B. In contrast to the wild type or an isogenic strain without the vacA gene, isogenic H. pylori strains with mutations in certain cag genes revealed only weak AP-1 and nuclear factor .kappa.B activation. In respect to the mol. components that direct AP-1 activity, our results indicate a cascade of the cellular stress response kinases c-Jun N-terminal kinase, MAP kinase kinase 4, and p21-activated kinase, and small Rho-GTPases including Rac1 and Cdc42, which contributes to the activation of proinflammatory cytokines/chemokines induced by H. pylori encoding the cag pathogenicity island.

REFERENCE COUNT: 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 36 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:709918 HCAPLUS
DOCUMENT NUMBER: 132:34431
TITLE: Urease-based mucosal immunization against **Helicobacter** heilmannii infection induces corpus atrophy in mice
AUTHOR(S): Dieterich, Christine; Bouzourene, Hanifa; **Blum, Andre L.**; **Corthesy-Theulaz, Irene E.**
CORPORATE SOURCE: Division of Gastroenterology, Centre Hospitalier Universitaire Vaudois, Lausanne, CH-1011, Switz.
SOURCE: Infection and Immunity (1999), 67(11), 6206-6209
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mucosal immunization with **Helicobacter** heilmannii urease B or H. pylori urease, given nasally with cholera toxin, protects BALB/c mice against H. heilmannii infection and reduces a preexisting infection. However, immunization aggravates **gastric** corpus atrophy. The authors' results underline the necessity of defining immunization regimens that do not enhance mucosal damage.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:428883 HCAPLUS
DOCUMENT NUMBER: 131:210809
TITLE: New inhibitors of **Helicobacter** pylori urease holoenzyme selected from phage-displayed peptide libraries
AUTHOR(S): Houimel, Mehdi; Mach, Jean-Pierre; **Corthesy-Theulaz, Irene**; Corthesy, Blaise; Fisch, Igor
CORPORATE SOURCE: Institute of Biochemistry, University of Lausanne, Epalinges, 1066, Switz.
SOURCE: European Journal of Biochemistry (1999), 262(3), 774-780
CODEN: EJBCAI; ISSN: 0014-2956
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Urease is an important virulence factor for **Helicobacter** pylori and is crit. for bacterial colonization of the human **gastric** mucosa. Specific inhibition of urease activity has been proposed as a possible strategy to fight this bacteria which infects billions of individual throughout the world and can lead to severe pathol. conditions in a limited no. of cases. We have selected peptides which specifically bind and inhibit H. pylori urease from libraries of random peptides displayed on filamentous phage in the context of pIII coat protein. Screening of a highly diverse 25-mer combinatorial library and two newly constructed random 6-mer peptide libraries on solid phase H. pylori urease holoenzyme allowed the identification of two peptides, 24-mer TFLPQPRCSALLRYLSEDGVIVPS and 6-mer YDFYWW that can bind and inhibit the activity of urease purified from H. pylori. These two peptides were chem. synthesized and their inhibition consts. (Ki) were found to be 47 .mu.M

for the 24-mer and 30 .mu.M for the 6-mer peptide. Both peptides specifically inhibited the activity of H. pylori urease but not that of Bacillus pasteurii.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:346011 HCAPLUS
DOCUMENT NUMBER: 131:17350
TITLE: Effect of whey-based culture supernatant of Lactobacillus acidophilus (johnsonii) La1 on **Helicobacter** pylori infection in humans
AUTHOR(S): **Michetti, Pierre**; Dorta, G.; Wiesel, P. H.; Brassart, D.; Verdu, E.; Herranz, M.; Felley, C.; Porta, N.; Rouvet, M.; **Blum, A. L.**; **Corthesy-Theulaz, I.**
CORPORATE SOURCE: Division Gastroenterology, Department Medicine, Univ. Lausanne, Lausanne, Switz.
SOURCE: Digestion (1999), 60(3), 203-209
CODEN: DIGEBW; ISSN: 0012-2823
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Specific strains of L. acidophilus are known to inhibit intestinal cell adhesion and invasion by enterovirulent bacteria. As L. acidophilus can survive transiently in the human stomach, it may down-regulate H. pylori infection. The ability of L. acidophilus (johnsonii) La1 supernatant to interfere with H. pylori bacterial growth, urease activity, and adhesion to epithelial cells was tested in vitro. Its effect on H. pylori infection in volunteers was monitored in a randomized, double-blind, controlled clin. trial, using a drinkable, whey-based, La1 culture supernatant. H. pylori infected volunteers were treated 14 days with 50 mL of La1 supernatant 4 .times. a day combined with either omeprazole 20 mg 4 .times. a day or with placebo. Infection was assessed by breath test, endoscopy, and biopsy sampling, performed at inclusion, immediately at the end of the treatment (breath test only), and 4 wk after the end of the treatment. La1 supernatant inhibited H. pylori growth in vitro, regardless of previous binding of H. pylori to epithelial cells. In 20 subjects (8 females, 12 males, mean age 33.1 yr) a marked decrease in breath test values was obsd. immediately after treatment with La1 supernatant, both in the omeprazole and in the placebo group (median 12.3 vs. 28.8 and 9.4 vs. 20.4, resp.). In both treatment groups, breath test values remained low 6 wk after treatment (omeprazole treated 19.2, placebo treated 8.3; vs. pretreatment), but the persistence of H. pylori infection was confirmed in **gastric** biopsies. La1 culture supernatant shown to be effective in vitro has a partial, acid-independent long-term suppressive effect on H. pylori in humans.
REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:210574 HCAPLUS
DOCUMENT NUMBER: 131:16185
TITLE: Genetic and functional characterization of the alpAB

gene locus essential for the adhesion of **Helicobacter** pylori to human **gastric** tissue
AUTHOR(S): Odenbreit, Stefan; Till, Markus; Hofreuter, Dirk; Faller, Gerhard; **Haas, Rainer**
CORPORATE SOURCE: Max-Planck-Institut fur Biologie, Tubingen, D-72076, Germany
SOURCE: Molecular Microbiology (1999), 31(5), 1537-1548
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In this study, we isolated and characterized a chromosomal locus of **Helicobacter** pylori previously identified by transposon shuttle mutagenesis as being involved in the adhesion of the pathogen to **gastric** epithelial cells. Two closely homologous genes were identified, designated as alpA and alpB, encoding outer membrane (OM) proteins of 518 amino acids each. They are members of the outer membrane protein supergene family identified in the H. pylori 26695 complete genome sequence. AlpA carries a functional lipoprotein signal sequence. AlpB carries a putative std. N-terminal signal sequence and shows a strong amino-acid sequence identity to AlpA. Transposon insertion mutagenesis, immunoblotting and primer extension studies indicate that both genes are organized in an operon, but no obvious consensus promoter sequence was found upstream of the transcriptional start site. The C-terminal portion of both proteins is predicted to form a porin-like .beta.-barrel in the outer membrane, consisting of 14 transmembrane amphipathic P-strands. Adhesion expts. with defined isogenic mutants indicate that both proteins are necessary for specific adherence of H. pylori to human **gastric** tissue. The pattern of AlpAB-dependent adherence of H. pylori to the **gastric** epithelial surface shows a clear difference to the BabA2-mediated adherence to Lewis, suggesting that a different receptor is involved.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 19 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:149566 HCAPLUS
DOCUMENT NUMBER: 131:13722
TITLE: Effects of pumaprazole (BY841), a novel reversible proton pump antagonist, and of omeprazole, on intragastric acidity before and after cure of **Helicobacter** pylori infection
AUTHOR(S): Martinek, J.; **Blum, A. L.**; Stolte, M.; Hartmann, M.; Verdu, E. F.; Luhmann, R.; Dorta, G.; Wiesel, P.
CORPORATE SOURCE: Division of Gastroenterology, CHUV, Lausanne, Switz.
SOURCE: Alimentary Pharmacology and Therapeutics (1999), 13(1), 27-34
CODEN: APTHEN; ISSN: 0269-2813
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Omeprazole produces a higher intragastric pH in the presence of

Helicobacter pylori infection than after cure. To investigate whether this effect also occurs with pumaprazole (BY841), a reversible proton pump antagonist which, in contrast to omeprazole, does not require activation in the acid compartment of the parietal cell. In a randomized, crossover, double-blind study. 24-H intragastric pH was measured in 13 H. pylori-pos. subjects before and after a 1-wk course of omeprazole (20 mg o.d.) or of pumaprazole (100 mg b.d.). The studies were repeated after the infection was cured. In the absence of drug administration, the median 24-h pH values before cure (median 2.0, 90% CI: 1.2-3.2) did not differ from those after cure (median 1.5, 90% CI: 1.3-2.2; P = 0.115). The 24-h pH values were higher before cure of the infection than after during both pumaprazole (6.0, 4.8-6.7 vs. 4.3, 2.6-5.7; P = 0.002) and omeprazole (5.8, 4.0-6.2 vs. 3.6, 2.8-5; P = 0.004). Both before and after cure, there were no significant differences between the two drugs with respect to acid inhibition over the 24-h period. The median decrease in acid inhibition after cure of the infection (calcd. as the difference in H+ activity in mmol/L) during pumaprazole (median 0.05, 90% CI: 6.times.10-4-2.3) was no different from that during omeprazole (median 0.2, 90% CI: 3.times.10-3-1.5; P = 0.6). Both before and after cure of H. pylori infection, pumaprazole raised the intragastric pH over a 24-h period to a similar degree as omeprazole. H. pylori infection similarly augments the pH-increasing effect of both drugs. This effect is related to H. pylori infection and not to an increased activation of acid inhibitory agents in the parietal cell compartment.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 20 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:664234 HCAPLUS
DOCUMENT NUMBER: 130:106751
TITLE: Properties and function of the P type ion pumps cloned from **Helicobacter** pylori
AUTHOR(S): Melchers, Klaus; Herrmann, Lutz; Mauch, Frieder; Bayle, Denis; Heuermann, Dorothee; Weitzenegger, Thomas; Schuhmacher, Alexander; Sachs, George; **Haas, Rainer**; Bode, Gunter; Bensch, Klaus; Schafer, Klaus P.
CORPORATE SOURCE: Department of Molecular Biology, Byk Gulden Pharmaceuticals, Konstanz, 78462, Germany
SOURCE: Acta Physiologica Scandinavica, Supplementum (1998), 163(643), 123-135
CODEN: APSSAD; ISSN: 0302-2994
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Three distinct P type pumps were cloned from H. pylori 69A. Two of these pumps, ATPase 439 and ATPase 948 (CopA), were isolated by gene library screening using DNA oligonucleotide primers. Amino acid similarities found for the predicted proteins were about 50% to Cd2+/Cu2+ pumps. Gene disruption mutagenesis rendered the H. pylori knockout mutants more sensitive to Zn2+ and Cd2+ (ATPase 439) or Cu2+ (CopA). Some of the ATPase 439-deficient mutants were neg. for urease activity while the majority of the mutants remained pos. Functional diversity of the pumps was also reflected by the ion affinities found for N-terminal peptides of

CopA to Cu2+ and of ATPase 439 to Ni2+, Cu2+ and Co2+. The membrane domain of the two pumps were exptl. shown to consist of eight membrane spans. When ATPase 439 was expressed under control of a tac promoter in Escherichia coli, vanadate-sensitive phosphate accumulation was obsd. cytochem. along the membrane of the host cells. The third P type pump (ATPase 115) which also exhibited homol. to transition metal ATPase was identified by sequencing a library of H. pylori membrane genes. The hydropathy plot of this pump was very similar to the former H. pylori ATPases, whereas the N-terminal ion binding region was distinct. It was concluded that, in H. pylori, the presence of three transition metal ATPases with distinct ion specificity contributes to the adaptive mechanisms for **gastric** survival.

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:380151 HCAPLUS
DOCUMENT NUMBER: 129:131899
TITLE: Natural competence for DNA transformation in **Helicobacter** pylori: identification and genetic characterization of the comB locus
AUTHOR(S): Hofreuter, Dirk; Odenbreit, Stefan; Henke, Gabriele; **Haas, Rainer**
CORPORATE SOURCE: Infektionsbiologie, Max-Planck-Institut for Biologie, Tobingen, D-72076, Germany
SOURCE: Molecular Microbiology (1998), 28(5), 1027-1038
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The Gram-neg. bacterial pathogen **Helicobacter** pylori, an important etiol. agent of **gastroduodenal** disease in humans, belongs to a group of bacterial species displaying competence for genetic transformation. Here, the authors describe the comb gene locus of H. pylori involved in DNA transformation competence. It consists of a cluster of four tandemly arranged genes with partially overlapping open reading frames, orf2, comB1, comB2 and comB3, constituting a single transcriptional unit. Orf2 encodes a 37-amino-acid peptide carrying a signal sequence, whereas comB1, comB2 and comB3 produce 29kDa, 38kDa and 42kDa proteins, resp., as demonstrated by immunoblotting with specific antisera. For Orf2 and ComB1, no homologous proteins were identified in the database. For ComB3, the best homologies were found with TraS/TraB from the Pseudomonas aeruginosa conjugative plasmid RP1 and Trbl of plasmid RP4, VirB10 from the Ti plasmid of Agrobacterium tumefaciens and PtIG, a protein involved in secretion of pertussis toxin of Bordetella pertussis. Defined transposon knock-out mutants in individual comb genes resulted in transformation-defective phenotypes ranging from a 90% redn. to a complete loss of the natural transformation efficiency. The comB2 and comB3 genes show homol. to HP0528 and HP0527, resp., located on the cagII pathogenicity island of H. pylori strain 26695.

L10 ANSWER 22 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:281567 HCAPLUS
DOCUMENT NUMBER: 129:91101

TITLE: Presence of multiple "**Helicobacter** heilmannii" strains in an individual suffering from **ulcers** and in his two cats
AUTHOR(S): Dieterich, Christine; Wiesel, Paul; Neiger, Reto; **Blum, Andre; Corthesy-Theulaz, Irene**
CORPORATE SOURCE: Division of Gastroenterology, Department of Medicine, Centre Hospitalier Universitaire Vaudois, Lausanne, CH-1011, Switz.
SOURCE: Journal of Clinical Microbiology (1998), 36(5), 1366-1370
CODEN: JCMIDW; ISSN: 0095-1137
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Circumstantial evidence suggests that "**Helicobacter** heilmannii" infection is an example of zoonosis. The presence of "H. heilmannii" strains in a human subject with acute **gastric** erosions, in his two cats, and in two unrelated cats was analyzed, and the genetic relatedness of the human and feline strains was assessed. A 580-bp, PCR-amplified sequence of "H. heilmannii" urease B gene (ureB) obtained from biopsies from the human subject and his two cats was restricted with AluI and cloned for sequencing. Anal. of the restriction fragment length polymorphism of the ureB-amplified product suggested the presence of different individual "H. heilmannii" strains in the cats and of three distinct strains in the human subject. One of the "H. heilmannii" ureB sequences amplified from the human subject's biopsies was identical to that derived from one of his cats. The degree of similarity between the other "H. heilmannii" human and feline nucleotide sequences was higher than 97%. Most of the base substitutions were conservative. We conclude that human and animal "H. heilmannii" strains are closely related and that humans can be infected by more than one "H. heilmannii" strain, as has been obsd. for **Helicobacter** pylori.

L10 ANSWER 23 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:2613 HCAPLUS
DOCUMENT NUMBER: 128:56914
TITLE: **Gastroenterology**. Part 2. Acid research and **ulcer** therapy
AUTHOR(S): Martinek, Jan; Koelz, Hans Rudolf; **Blum, Andre L.**
CORPORATE SOURCE: Division Gastro-Enterologie, Centre Hospitalier, Universitaire Vaudois, Lausanne, CH-1011, Switz.
SOURCE: Arzneimittel-Forschung (1997), 47(12), 1424-1435
CODEN: ARZNAD; ISSN: 0004-4172
PUBLISHER: Editio Cantor Verlag
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB Three discoveries of the last thirty years have revolutionized acid research and **ulcer** therapy: H2-receptors and their competitive inhibition, the acid pump and its blockade and, finally, **Helicobacter** pylori and its central role in **ulcer** disease. Today the problem of **ulcer** treatment is more or less solved by the correct use of antibiotics, while the cure of reflux disease is still problematic: pump blockers accelerate the healing of mucosal

breaks and prevent, when given at long term, recurrences but they cannot change the natural history of reflux disease. These facts form the basis for future research. This article is reviewed by 112 refs.

L10 ANSWER 24 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:684504 HCAPLUS
DOCUMENT NUMBER: 127:356945
TITLE: Polyhydroxybutrate biosynthetic enzymes of **Helicobacter** for use as targets in the diagnosis and treatment of **gastrointestinal** disease
INVENTOR(S): **Corthesy-Theulaz, Irene**
PATENT ASSIGNEE(S): Kieta Holdings S.A., Switz.; Corthesy-Theulaz, Irene
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9738110	A2	19971016	WO 1997-IB409	19970403
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9723040	A1	19971029	AU 1997-23040	19970403
EP 904381	A2	19990331	EP 1997-915631	19970403
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6060241	A	20000509	US 1997-834776	19970403

PRIORITY APPLN. INFO.: US 1996-14906P P 19960405
WO 1997-IB409 W 19970403

AB A poly-3-hydroxybutyrate metabolic pathway essential for **Helicobacter** pylori survival in a host is described for use as a target in the diagnosis and treatment of infection. A novel CoA transferase ((Hp)CoA-t), thiolase and PHB synthase are described and genes encoding the (Hp) CoA-t and thiolase are cloned and methods for detecting the genes and the enzymes are described. Methods for the detn. of a propensity to develop **gastritis**, peptic **ulcer** disease, or **gastric** cancer is provided for by detection methods. Methods are also provided for the use of (Hp) CoA-t, thiolase or PHB synthase proteins and fragments retaining enzymic activity in the identification of potential drug candidates for the treatment of some types of **gastric** disease. Pharmaceutical compns. contg. (Hp) CoA-t protein fragments, antisense nucleic acids or other inhibitors of (Hp) CoA-t, thiolase and PHB synthase as well as methods for their use in the treatment of some types of **gastric** disease are also provided. Cloning and expression of the genes in Escherichia coli is described. H.

pylori mutants lacking one of the subunits of the CoA transferase were constructed by std. methods were unable to colonize germ-free BALB/c mice.

L10 ANSWER 25 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:560101 HCAPLUS
DOCUMENT NUMBER: 127:229261
TITLE: Effect of curing **Helicobacter** pylori infection on intragastric acidity during treatment with ranitidine in patients with duodenal **ulcer**
AUTHOR(S): Labenz, J.; Tillenburg, B.; Peitz, U.; Verdu, E.; Stolte, M.; Borsch, G.; **Blum, A. L.**
CORPORATE SOURCE: Department of Internal Medicine and Gastroenterology, Elisabeth Hospital, Essen, D-45138, Germany
SOURCE: Gut (1997), 41(1), 33-36
CODEN: GUTTAK; ISSN: 0017-5749
PUBLISHER: BMJ Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In patients with duodenal **ulcer** cure of **Helicobacter** pylori infection resulted in a pronounced decrease in intragastric pH during treatment with omeprazole. Our aim was to test the hypothesis that treatment of H pylori adversely affects the pH response to ranitidine. Eighteen patients with duodenal **ulcer** who were infected with H pylori were studied. Twenty four hour pH recordings were performed during treatment with ranitidine (300 mg) at night before and four to six weeks after cure of H pylori infection. Presence of H pylori was assessed by a rapid urease test, culture, histol., and a 13C urea breath test. Also, the fasting **gastrin** concns. were measured before and after treatment for H pylori infection. Cure of H pylori infection resulted in a considerable improvement in both antral and corpus **gastritis** and a decrease in fasting **gastrin** concns. As a result of the cure the night time intragastric pH during treatment with ranitidine decreased (median pH 6.8 .nu. 5.4; p=0.007), whereas the acidity during the daytime was not affected. In patients with duodenal **ulcer** the intragastric pH during treatment with ranitidine depends on H pylori. However, the loss of effectiveness in altering pH seems to be less pronounced than previously found with omeprazole.

L10 ANSWER 26 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:325719 HCAPLUS
DOCUMENT NUMBER: 127:48538
TITLE: MALT-type lymphoma of the stomach is associated with **Helicobacter** pylori strains expressing the CagA protein
AUTHOR(S): Eck, Matthias; Schmauer, Bernd; **Haas, Rainer**; Greiner, Axel; Czub, Stefanie; Mueller-Hermelink, Hans Konrad
CORPORATE SOURCE: Institut fur Pathologie, Universitat Wurzburg, Wurzburg, Germany
SOURCE: Gastroenterology (1997), 112(5), 1482-1486
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: Saunders
DOCUMENT TYPE: Journal

LANGUAGE: English
AB **Helicobacter** pylori is considered to be involved in the pathogenesis of **gastric** lymphoma of mucosa-assocd. lymphoid tissue (MALT) type. Strains expressing the CagA protein (CagA+ strains) have been strongly assocd. with severe **gastritis**, duodenal **ulceration**, and **gastric** adenocarcinoma. The aim of this study was to det. the presence of H. pylori as well as incidence of CagA+ strains in **gastric** MALT-type lymphoma. Sera of 68 patients with **gastric** MALT-type lymphoma (22 with low grade, 36 with high grade, and 10 with secondary high grade) were obtained, and the serol. response to CagA was studied by immunoblotting using a purified recombinant CagA protein, a CagA+ strain, and the corresponding isogenic CagA- mutant. Of the patients with MALT-type lymphoma, 98.5% (67 of 68 patients) were H. pylori seropos. In the only seroneg. patient, the bacterium was detected histol. by Warthin-Starry staining. Of the seropos. patients, 95.5% had serum IgG antibodies to CagA compared with 67% of an H. pylori-pos. control group (33 of 49 patients; P = 0.000037) with chronic active **gastritis**. These results indicate infection of almost all patients with MALT-type lymphoma by CagA+ H. pylori strains. Strains expressing the CagA protein seem to play a crucial role in the pathogenesis of **gastric** MALT-type lymphoma.

L10 ANSWER 27 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:317123 HCAPLUS
DOCUMENT NUMBER: 126:338649
TITLE: Efficacy of omeprazole one year after cure of **Helicobacter** pylori infection in duodenal **ulcer** patients
AUTHOR(S): Labenz, Joachim; Tillenburg, Birgit; Peitz, Ulrich; Boersch, Gereon; Idstroem, Jan-Peter; Verdu, Elena; Stolte, Manfred; **Blum, Andre L.**
CORPORATE SOURCE: Department of Internal Medicine and Gastroenterology, Elisabeth Hospital Essen, Germany
SOURCE: American Journal of Gastroenterology (1997), 92(4), 576-581
CODEN: AJGAAR; ISSN: 0002-9270
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have previously shown that, in duodenal **ulcer** patients, pH control by omeprazole is less pronounced after cure of **Helicobacter** pylori infection. The present study was designed to test the hypothesis that this response to omeprazole persists 1 yr after cure of H. pylori infection. In 12 duodenal **ulcer** patients, intragastric acidity was measured with a glass electrode during treatment with omeprazole (20 mg) once daily before, and 4-6 wk and 1 yr after, cure of H. pylori infection. H. pylori infection was assessed by [13C]urea breath test, culture, histol. (Warthin Starry stain), and rapid urease test. Cure of H. pylori infection resulted in a lowered pH during omeprazole treatment. This effect persisted after 1 yr. Median 24-h **gastric** pH before H. pylori treatment was 5.6; 4-6 wk after cure of the infection it was 2.9 (p = 0.003), and 1 yr after cure of the infection it remained unchanged (pH = 2.5; p = 0.5). Accordingly, twice as much time was spent above pH 3 and pH 4 before H. pylori treatment than

1 or 12 mo after cure (percent of time .gtoreq. pH 3: 82.7 vs. 49.7 vs. 43.1; percent of time .gtoreq. pH 4: 72.7 vs. 38.3 vs. 26.4). In duodenal **ulcer** patients, cure of H. pylori infection resulted in a marked rapid and persistent decrease of the pH increasing effect of omeprazole. Therefore, H. pylori is a determinant of the pH achieved in response to omeprazole treatment in duodenal **ulcer** patients.

L10 ANSWER 28 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:274424 HCAPLUS
DOCUMENT NUMBER: 126:342542
TITLE: The selection of dairy bacterial strains with probiotic properties based on their adhesion to human intestinal epithelial cells
AUTHOR(S): Brassart, D.; Neeser, J.-R.; **Michetti, P.**; Servin, A. L.
CORPORATE SOURCE: Nestle Research Center, Lausanne, Switz.
SOURCE: Bacteries Lactiques, Actes du Colloque LACTIC 94, Caen, Fr., Sept. 7-9, 1994 (1995), Meeting Date 1994, 201-212. Editor(s): Novel, Georges; Le Querler, Jean-Francois. Presses Universitaires de Caen: Caen, Fr.
CODEN: 64HMA5
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB Lactic acid bacteria (LAB), in certain fermented milks, survive intestinal transit in the human and exert beneficial biol. effects (probiotic effects) therein. Since such bacteria does not permanently colonize the human intestine, it is desirable to select strains better adapted to this ecosystem. Adhesion to human intestinal epithelial cells is a criteria worthy of consideration. The use of the differentiated human intestinal epithelial cell lines, HT-29 and Caco-2, in the selection of adherent human strains from the Nestec collection was reported. Adhesion, although not a general feature of LAB seems mediated, at least with respect to Lb. acidophilus LA1 and three bifidobacterial strains (Bbr4, Bl16, Bi1), through adhesion-promoting protein(s). Also, LA1 significantly inhibits cell adhesion and/or cell invasion by pathogenic Escherichia coli, Salmonella typhimurium, or Yersinia pseudotuberculosis. In addn., LA1 similarly affects **Helicobacter** pylori, the **ulcer** assocd. bacterium. Comparable results were obtained with adherent human bifidobacteria. All this was discussed with 20 refs.

L10 ANSWER 29 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:23697 HCAPLUS
DOCUMENT NUMBER: 126:69765
TITLE: Intragastric pH during treatment with omeprazole: Role of **Helicobacter** pylori and H, pylori-associated **gastritis**
AUTHOR(S): Verdu, E. F.; Armstrong, D.; Idstrom, J.-P.; Labenz, J.; Stolte, M.; Borsch, G.; **Blum, A. L.**
CORPORATE SOURCE: Division Gastroenterology, CHUV, Lausanne, Switz.
SOURCE: Scandinavian Journal of Gastroenterology (1996), 31(12), 1151-1156
CODEN: SJGRA4; ISSN: 0036-5521
PUBLISHER: Scandinavian University Press

DOCUMENT TYPE: Journal
LANGUAGE: English
AB Omeprazole treatment produces lower intragastric pH values 4 wk after cure of **Helicobacter** pylori infection than before. The authors therefore investigated the effect of healing H. pylori-assocd. **gastritis** on intragastric pH in the presence and in the absence of omeprazole therapy. Before and on day 8 of omeprazole, 20 mg once daily, 24-h intragastric pH-recordings were performed in 14 subjects with H. pylori infection and repeated 4 and 52 wk after cure of infection. **Gastritis** severity in corpus and antrum was graded by using a modified Sydney system. In the absence of omeprazole administration, median 24-h pH values before cure did not differ from those 4 and 52 wk after cure. On day 8 of omeprazole administration, 24-h pH values were much higher before cure (median, 5.15; 95% confidence interval (CI), 4.3-6.0) than 4 wk (3.6; 2.1-4.4) and 52 wk after cure (3.0; 2.1-4.4). The activity of corpus and antral **gastritis** was not assocd. with the magnitude of H+ change induced by omeprazole. The increased pH produced by omeprazole during H. pylori infection is likely to be due to neutralizing substances produced by H. pylori and not to H. pylori-induced **gastritis**.

L10 ANSWER 30 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:532139 HCAPLUS
DOCUMENT NUMBER: 125:185471
TITLE: Effects of misoprostol on healing and prevention of biopsy-induced **gastroduodenal** lesions occurring during the administration of diclofenac to volunteers
AUTHOR(S): Dorta, G.; Nicolet, M.; Vouillamoz, D.; Margalith, D.; **Blum, A. L.**; Armstrong, D.
CORPORATE SOURCE: Division de Gastroenterologie, CHUV, Lausanne, 1011, Switz.
SOURCE: Aliment. Pharmacol. Ther. (1996), 10(4), 563-569
CODEN: APTHEN; ISSN: 0269-2813
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To det. whether misoprostol promotes the healing of non-steroidal anti-inflammatory drug induced **gastroduodenal** lesions in a human exptl. model. Mucosal damage and healing of mucosal biopsy sites were assessed endoscopically in 10 healthy, **Helicobacter** pylori-neg. volunteers with a normal initial endoscopy: they were enrolled in a double-blind, double-dummy, placebo-controlled cross-over study. They received 2-wk courses of misoprostol (200 .mu.g b.d.) or placebo: a water-sol. non-steroidal antiinflammatory drug diclofenac 50 mg t.d.s., was given during the second week of each dosage regimen after three endoscopic biopsies had been taken from each of the duodenum, antrum and corpus. The no. of unhealed biopsy sites was not different after misoprostol or placebo, although the no. of healed biopsy sites was greater in the corpus and duodenum than in the antrum. Misoprostol did not prevent the appearance of diclofenac-induced erosions and petechiae. Epigastric discomfort was related to the intake of diclofenac and was reduced by misoprostol. Bloating and flatulence occurred more frequently with misoprostol alone and with misoprostol plus diclofenac, than with placebo alone or placebo plus diclofenac. Misoprostol does not prevent

new mucosal lesions induced by diclofenac in healthy volunteers and it does not accelerate the healing of the biopsy sites. Misoprostol decreases the frequency of diclofenac induced epigastric discomfort, but it increases gas bloating and flatulence.

L10 ANSWER 31 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:286501 HCAPLUS
DOCUMENT NUMBER: 125:2539
TITLE: Optimized BlaM-transposon shuttle mutagenesis of **Helicobacter** pylori allows the identification of novel genetic loci involved in bacterial virulence
AUTHOR(S): Odenbreit, Stefan; Till, Markus; **Haas, Rainer**
CORPORATE SOURCE: Max-Planck-Institut Biologie, Abteilung Infektionsbiologie, Tuebingen, D-72076, Germany
SOURCE: Mol. Microbiol. (1996), 20(2), 361-373
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Helicobacter** pylori is an important etiol. agent of **gastroduodenal** disease in humans. This report describes a general genetic approach for the identification of genes encoding exported proteins in H. pylori. The novel TnMax9 mini-blaM transposon was used for insertion mutagenesis of a H. pylori gene library established in Escherichia coli. A total of 192 E. coli clones expressing active .beta.-lactamase fusion proteins (BlaM+) were obtained, indicating that the corresponding target plasmids carry H. pylori genes encoding putative extracytoplasmic proteins. Natural transformation of H. pylori P1 or P12 using the 192 mutant plasmids resulted in 135 distinct H. pylori mutant strains (70%). Screening of the H. pylori collection of mutant strains allowed the identification of mutant strains impaired in motility, in natural transformation competence, and in adherence to **gastric** epithelial cell lines. Motility mutants could be grouped into distinct classes: (i) mutant strains lacking the major flagellin subunit FlaA and intact flagella (class I); (ii) mutant strains with apparently normal flagella, but reduced motility (class II), and (iii) mutant strains with obviously normal flagella, but completely abolished motility (class III). Two independent mutations that exhibited defects in natural competence for genetic transformation mapped to different genetic loci. In addn., 2 independent mutant strains were isolated by their failure to bind to the human **gastric** carcinoma cell line KatoIII. Both mutant strains carried a transposon in the same gene, 0.8 kb apart, and showed decreased autoagglutination when compared to the wild-type strain.

L10 ANSWER 32 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:194569 HCAPLUS
DOCUMENT NUMBER: 124:278684
TITLE: **Helicobacter** pylori augments the pH-increasing effect of omeprazole in patients with duodenal **ulcer**
AUTHOR(S): Labenz, Joachim; Tillenburg, Birgit; Peitz, Ulrich; Idstroem, Jan-Peter; Verdu, Elena F.; Stolte, Manfred; Boersch, Gereon; **Blum, Andre L.**
CORPORATE SOURCE: Department Internal Medicine and Gastroenterology, Elisabeth Hospital, Essen, Germany

SOURCE: Gastroenterology (1996), 110(3), 725-32
CODEN: GASTAB; ISSN: 0016-5085

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Omeprazole is less effective in healthy subjects than in patients with duodenal **ulcers**. The aim of this study was to det. whether **Helicobacter** pylori augments the pH-increasing effect of omeprazole in patients with duodenal **ulcers**. In 16 patients with duodenal **ulcers**, baseline intragastric acidity was measured before and 4-6 wk after the cure of H. pylori infection. In 17 patients with duodenal **ulcers**, 24-h pH metry was performed during treatment with 20 mg omeprazole once daily before as well as after eradication of H. pylori. Intragastric acidity was measured using a glass electrode placed 5 cm below the cardia. H. pylori infection was assessed by [13C] urea breath test, culture, histol., and rapid urease test. H. pylori eradication resulted in a marked decrease of the pH-increasing effect of omeprazole (24-h median **gastric** pH, 5.5 vs. 3.0; P < 0.002) that was most pronounced during nighttime (median **gastric** pH, 6.4 vs. 2.1; P = 0.001). On the other hand, baseline intragastric pH remained unchanged after eradication (median **gastric** pH, 1.0 vs. 1.1; P = 0.5). In patients with duodenal **ulcers** treated with omeprazole, intragastric pH depends significantly on the presence or absence of H. pylori, whereas baseline pH remained unchanged after H. pylori eradication.

L10 ANSWER 33 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:69418 HCAPLUS
DOCUMENT NUMBER: 124:193910
TITLE: Effect of curing **Helicobacter** pylori infection on intragastric pH during treatment with omeprazole
AUTHOR(S): Verdu, E F; Armstrong, D; Idstrom, J-P; Labenz, J; Stolte, M; Dorta, G; Borsch, G; **Blum, A L**
CORPORATE SOURCE: Division de Gastroenterologie, CHUV, Lausanne, 1011, Switz.
SOURCE: Gut (1995), 37(6), 743-8
CODEN: GUTTAK; ISSN: 0017-5749

DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has been shown that omeprazole treatment produces higher intragastric pH values in **Helicobacter** pylori pos. subjects than in H pylori neg. subjects. This study aimed to investigate the effect of curing H pylori on the intragastric pH in both the presence and absence of omeprazole therapy. Twenty four hour intragastric pH recordings were performed before and after a one week course of omeprazole (20 mg once daily) in 18 H pylori pos. subjects and were repeated after the infection had been cured. In the absence of omeprazole, the total 24 h pH values before cure did not differ from those afterwards. During omeprazole treatment the 24 h pH values were much higher before (median 95% CI), than after cure of infection ($p<0.001$). The omeprazole induced fall in H+ activity before cure of H pylori did not, however, differ from that afterwards. It is concluded that the apparently greater antisecretory effect of omeprazole during H pylori infection may be a result of the prodn. of acid neutralizing compds. by the H pylori. Although a direct

interaction between H pylori and omeprazole cannot be excluded, it seems unlikely.

L10 ANSWER 34 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:852008 HCAPLUS
DOCUMENT NUMBER: 123:237791
TITLE: Urease-based vaccine and treatment for **Helicobacter** infection
INVENTOR(S): **Michetti, Pierre**; Corthesy-Theulaz, Irene; Blum, Andre; Davin, Catherine; Haas, Rainer; Kraehenbuhl, Jean-Pierre; Saraga, Emilia
PATENT ASSIGNEE(S): Oravax, Inc., USA
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9522987	A1	19950831	WO 1995-US2202	19950223
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6290962	B1	20010918	US 1994-200346	19940223
AU 9519681	A1	19950911	AU 1995-19681	19950223
AU 694195	B2	19980716		
EP 751786	A1	19970108	EP 1995-912583	19950223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9506884	A	19970819	BR 1995-6884	19950223
JP 09509661	T2	19970930	JP 1995-522429	19950223
PL 179149	B1	20000731	PL 1995-316007	19950223
NO 9603508	A	19961021	NO 1996-3508	19960822
FI 9603281	A	19961022	FI 1996-3281	19960822

PRIORITY APPLN. INFO.:

US 1994-200346	A	19940223
US 1992-970996	B2	19921103
US 1993-85938	A2	19930706
WO 1995-US2202	W	19950223

AB A method of eliciting in a mammalian host a protective immune response to **Helicobacter** infection and treatment of **Helicobacter** infection by administering to the host an immunogenically effective amt. of a **Helicobacter** urease or urease subunits as antigen is described. Vaccine compns. are also provided.

L10 ANSWER 35 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:451085 HCAPLUS
DOCUMENT NUMBER: 121:51085
TITLE: Genetic analysis of the **Helicobacter** pylori vacuolating cytotoxin: structural similarities with

the IgA protease type of exported protein
AUTHOR(S): Schmitt, Wolfgang; **Haas, Rainer**
CORPORATE SOURCE: Abt. Infektionsbiol., Max-Planck-Inst. Biol., Tuebingen, D-72076, Germany
SOURCE: Mol. Microbiol. (1994), 12(2), 307-19
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The human **gastric** bacterial pathogen **Helicobacter** pylori has been implicated in type B **gastritis**, peptic **ulceration** and **gastric** adenocarcinoma. Here the authors report on the cloning and genetic characterization of an H. pylori gene named vacA, which encodes the vacuolating cytotoxin VacA, a novel type of antigenic bacterial toxin that induces the formation of intracellular vacuoles in epithelial cells. The vacuolating cytotoxin activity is expressed by a subset of clin. isolates (Vac+), all of which produce the 87 kDa cytotoxin antigen, but strains which produce neither the activity nor the cytotoxin protein (Vac-) also carry the gene. Isogenic H. pylori mutants in vacA generated by transposon shuttle mutagenesis produce neither the VacA antigen nor a vacuolating activity in a cell culture model. The vacA gene itself encodes a precursor protein of 139.6 kDa consisting of a 33-amino acid signal sequence, the 87 kDa cytotoxin and a 50 kDa C-terminal domain with features typical of a bacterial outer membrane protein. The VacA precursor shows no significant primary sequence homol. with any previously reported protein, but its structural organization closely resembles the IgA protease-type of exoprotein produced by pathogenic Neisseriae and Haemophilus species. The authors' current data support a model for secretion of the cytotoxin through the two bacterial membranes which involves the 30 kDa domain for outer membrane translocation with subsequent proteolytic cleavage and release of the mature 87 kDa cytotoxin into the extracellular environment.

L10 ANSWER 36 OF 36 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:487670 HCAPLUS
DOCUMENT NUMBER: 119:87670
TITLE: Cloning and genetic characterization of a **Helicobacter** pylori flagellin gene
AUTHOR(S): Leying, H.; Suerbaum, S.; Geis, G.; **Haas, R.**
CORPORATE SOURCE: Abt. Infektionsbiol., Max-Planck-Inst. Biol., Tuebingen, D-7400, Germany
SOURCE: Mol. Microbiol. (1992), 6(19), 2863-74
CODEN: MOMIEE; ISSN: 0950-382X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Helicobacter** pylori produces polar sheathed flagella, which are believed to be essential for the bacterial colonization of the human **gastric** mucosa. Here the authors report on the cloning and genetic characterization of a H. pylori gene encoding the subunit of the flagellar filament, the flagellin. Screening of a genomic library of H. pylori with an oligonucleotide probe derived from the N-terminal amino acid sequence of purified flagellin resulted in a recombinant plasmid clone carrying the flagellin-encoding gene flaA on a 9.3 kb BglII fragment. The nucleotide sequence of flaA revealed an open reading frame of 1530 nucleotides, encoding a protein with a predicted mol. mass of 53.2

kDa, which is similar in size with the purified flagellin protein in SDS-polyacrylamide gel electrophoresis. Sequence alignment of H. pylori flagellins demonstrates a high degree of similarity in the amino-terminal and carboxy-terminal regions, including those of the closely related genus Campylobacter (56% overall identity with Campylobacter coli flaA), but little homol. in the central domain. Southern hybridizations of chromosomal DNA with flaA-specific probes did not reveal the presence of addnl. homologous flagellin genes in H. pyrlori. Sequence anal. of the flaA flanking regions and mapping of the flaA mRNA start site by a primer extension expt. indicated that transcription of the gene is under the control of a .sigma.28-specific promoter sequence in H. pylori. The region upstream of the flaA promoter is subject to local DNA modification, resulting in the masking of two out of three closely linked HindIII restriction sites in the chromosome of strain 898-1. Escherichia coli strains harboring the recombinant plasmid did not produce full-length flagellin and data obtained with FlaA fusion proteins using an E. coli plasmid expression system suggest that a distinct nucleotide sequence in the gene interferes with productive translation of this protein in E. coli.

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FILE LAST UPDATED: 22 Jul 2002 (20020722/ED)

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=> d stat que
L1 9858 SEA FILE=REGISTRY HELICOBACTER/BI
L2 461 SEA FILE=REGISTRY UREASE/BI
L3 1 SEA FILE=REGISTRY "CAGA PROTEIN (HELICOBACTER PYLORI GENE CAGA)"/CN
L4 1 SEA FILE=REGISTRY "UREASE B (HELICOBACTER PYLORI STRAIN HPK5 GENE UREB)"/CN
L5 6043 SEA FILE=HCAPLUS L1 OR L2 OR L3 OR L4 OR (H OR HELICOBACTER?)(W)UREASE?
L6 1488 SEA FILE=HCAPLUS VACCIN? AND (?GASTR? OR ULCER? OR ?DYSPEPSIA? OR METAPLASIA OR ?LYMPHOMA?)
L7 63 SEA FILE=HCAPLUS L5 AND L6

=> d ibib abs hitrn l7 1-63

L7 ANSWER 1 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:504552 HCAPLUS
TITLE: HP30 and HP56 genes and proteins from Helicobacter pylori and their use to induce immune responses to Helicobacter cells or antigens
INVENTOR(S): Tian, Jing-Hui; Walker, Richard; Jackson, W. James
PATENT ASSIGNEE(S): Antex Biologics, Inc., USA
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002051237 A2 20020704 WO 2001-US48392 20011207
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 2000-732091 A 20001207

AB The invention discloses Helicobacter pylori HP30 or HP56 polypeptide, polypeptides derived thereof (HP30-derived or HP56-derived polypeptides), nucleic acids encoding said polypeptides, antibodies that specifically bind the HP30, HP56, HP30-derived or HP56-derived polypeptides, and T cells specific for HP30, HP56, HP30-derived or HP56-derived polypeptide. Also disclosed are prophylactic or therapeutic compns., including immunogenic compns., e.g. **vaccines**, comprising HP30, HP56, HP30-derived or HP56-derived polypeptides, nucleic acids encoding the same or antibodies thereto. The invention addnl. discloses methods of inducing in animals an immune response to Helicobacter cells or antigens. Recombinant HP30 and HP56 show to ability to act as therapeutic agents to decrease or eliminate H. pylori colonization in mice previously infected with H. pylori. Fifty percent or more of animals **vaccinated** orally with recombinant HP30 and HP56 are protected against subsequent H. pylori **gastric** colonization, and the remaining animals are colonized at lower levels than mice immunized with crude H. pylori cell lysate.

IT **9002-13-5**, Urease
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**vaccine** immunogens; HP30 and HP56 genes and proteins from Helicobacter pylori and their use to induce immune responses to Helicobacter cells or antigens)

L7 ANSWER 2 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:391748 HCAPLUS
DOCUMENT NUMBER: 136:400601
TITLE: Helicobacter pylori gene hcpA and cysteine rich protein A and diagnostic and therapeutic uses thereof
INVENTOR(S): Deml, Ludwig; Schneider, Wulf; Lehn, Norbert
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002040516	A2	20020523	WO 2001-DE4303	20011115

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2000-10056486 A 20001115

AB The H. pylori gene hcpA and two proteins encoded by this gene are disclosed. The nucleic acids and proteins may be used for diagnosis of H. pylori infection and for prevention of infection, e.g., by **vaccination**. Thus, HcpA was shown to be immunogenic in humans and to be useful as a diagnostic marker of H. pylori infection. HcpA-producing H. pylori induced a strong interferon .gamma. release in murine spleen cell cultures; knockout hcpA mutants of H. pylori did not. The HcpA mRNA contained an internal translation start codon which overlapped the signal peptide cleavage site region. The majority of H. pylori strains studied expressed the hcpA gene, but secretion of HcpA into the culture was strain-dependent. Secretion of HcpA was not dependent on the sec path nor the Cag app. The anti-H. pylori antibody titer correlated with the HcpA secretion. HcpA was strongly secreted in **ulcer** patients. The HcpA protein contains a coiled-coil C-terminus which may influence its export from the cell.

IT **428657-62-9 428657-64-1 428657-66-3 428657-68-5 428657-70-9**
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; Helicobacter pylori gene hcpA and cysteine rich protein and diagnostic and therapeutic uses thereof)

IT **428657-61-8 428657-63-0 428657-65-2 428657-67-4 428657-69-6**
RL: DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; Helicobacter pylori gene hcpA and cysteine rich protein and diagnostic and therapeutic uses thereof)

L7 ANSWER 3 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:51293 HCAPLUS
DOCUMENT NUMBER: 136:107468
TITLE: Improvement of oral **vaccines**
INVENTOR(S): Bumann, Dirk; Meyer, Thomas F.
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Foerderung der Wissenschaften e.V., Germany
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004017	A2	20020117	WO 2001-EP7784	20010706

W: CA, JP, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

PRIORITY APPLN. INFO.: EP 2000-114683 A 20000707

AB The present invention relates to a method for prepg. and improving oral **vaccines** by modifying polypeptides which comprise at least one immunogenic epitope, particularly at least one immunogenic T cell epitope. Mice were **intragastrically** immunized with 5 mg ovalbumin in 100 .mu.L phosphate-buffered saline contg. 3% sodium bicarbonate with 10.000 U cholera toxoid.

IT **9002-13-5**, Urease
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A and B; improvement of oral **vaccines**)

L7 ANSWER 4 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:830481 HCAPLUS
DOCUMENT NUMBER: 136:100739
TITLE: Helicobacter pylori infection, immune response and **vaccination**
AUTHOR(S): Lembo, A.; Caradonna, L.; Magrone, T.; Mastronardi, M. L.; Caccavo, D.; Jirillo, E.; Amati, L.
CORPORATE SOURCE: Max Planck Institut fur Immunbiologie, Freiburg I. B., Germany
SOURCE: Current Drug Targets: Immune, Endocrine and Metabolic Disorders (2001), 1(3), 199-208
CODEN: CDTIBT; ISSN: 1568-0088
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. It is well known that abnormal immune responses may play a pathogenic role in the H. pylori-related **gastropathy**. Indeed, as far as humoral immune response is concerned, it is still debated whether specific anti-H. pylori antibodies have a protective or noxious effect in infected hosts. Besides proinflammatory cytokines released from macrophages, such as tumor-necrosis factor-.alpha. and interleukin-1.beta., and IFN-.gamma. derived from T-helper 1 lymphocytes, also interleukin-10, a product of T-helper 2 lymphocytes with antiinflammatory properties, seems to be surprisingly involved in the pathogenesis of H. pylori-induced **gastritis**. In addn., lipopolysaccharide derived from the outer membrane of H. pylori acts as a chemoattractant for monocytes and induces release of free radicals, interleukin-1.beta., interleukin-6, interleukin-8 and tumor necrosis factor-.alpha.. On the other hand, H. pylori lipopolysaccharide could be responsible for the increased polyamine concns. in the **gastric** mucosa and polyamines, such as putrescine, spermidine and spermine, could be involved in the increased cell proliferation and consequent possible neoplastic transformation of the **gastric** mucosa. Incubation of peripheral blood mononuclear cells with H. pylori increases significantly the surface expression of CD95 receptor (Fas), thus suggesting that these bacteria are able to induce apoptosis. In animal models, different types of **vaccination** have been investigated, including stimulation of nasal and rectal lymphoid tissue, as well as adoptive transfer of T cell from donors immunized with H. pylori. However, results obtained are frequently disappointing. In humans, urease of H. pylori was safely used as oral **vaccine** in the absence or presence of adjuvants with encouraging results. Finally, DNA **vaccines** could offer in the future advantages for prophylactic H. pylori eradication, esp. where population is infected by this microorganism since childhood.
IT **9002-13-5**, Urease
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(Helicobacter; Helicobacter pylori infection, immune response and **vaccination**)
REFERENCE COUNT: 93 THERE ARE 93 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:816711 HCAPLUS
DOCUMENT NUMBER: 135:356756
TITLE: Helicobacter antigens
INVENTOR(S): Meyer, Thomas F.; Jungblut, Peter; Bumann, Dirk; Aebischer, Anton; Haas, Gaby; Zimny-Arndt, Ursula; Lamer, Stephanie; Karaali, Galip; Sabarth, Nicolas; Wendland, Meike
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft Zur Foerderung Der

Wissenschaften E.V., Germany; et al.
SOURCE: PCT Int. Appl., 150 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001083531	A1	20011108	WO 2001-EP4728	20010426

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2000-108968 A 20000427
EP 2001-1101439 A 20010123

AB Using proteomics, the authors disclose the identification of proteins expressed by cultivated Helicobacter cells and which preferably react with human antisera. These Helicobacter antigens are provided which are suitable as targets for the diagnosis, prevention or treatment of Helicobacter infections.

IT **9002-13-5**, Urease
RL: ANT (Analyte); ANST (Analytical study)
(proteomic anal. of Helicobacter pylori proteins and antigens)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 6 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:300853 HCAPLUS
DOCUMENT NUMBER: 134:325198
TITLE: Treatment and prevention of Helicobacter infection with C-terminal fragments of recombinant Helicobacter catalase
INVENTOR(S): Doidge, Christopher Vincent; Webb, Elizabeth Ann; Rothel, Linda Joy; Sutton, Philip; Hazell, Stuart Lloyd
PATENT ASSIGNEE(S): Csl Limited, Australia; The University of New South Wales
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001029198	A1	20010426	WO 2000-AU1249	20001013

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1222255 A1 20020717 EP 2000-969109 20001013
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL
PRIORITY APPLN. INFO.: AU 1999-3471 A 19991015
WO 2000-AU1249 W 20001013

AB An isolated polypeptide and immunogenic fragments thereof are described together with their variants and derivs. as novel immunogenic agents for treating or preventing Helicobacter infection in a mammalian host. The polypeptide comprises a C-terminal portion of a Helicobacter catalase (strain RU1 and strain HP921023), which portion lacks significant amino acid sequence identity with human catalase, wherein the polypeptide is other than full-length Helicobacter catalase. The antigenic prepn. comprising the C-terminal fragment of catalase is used in a **vaccine** compn. for oral, intranasal or **intragastric** administration which includes a mucosal adjuvant and Helicobacter lipopolysaccharide or urease. Helicobacter catalase may be administered as the sole active immunogen in a **vaccine** compn. or expressed by alive vector. Thus, recombinant catalase shown to be an effective protective antigen for immunization against H. pylori infection.

IT **336208-60-7P 336208-61-8P**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; treatment and prevention of Helicobacter infection with C-terminal fragments of recombinant Helicobacter catalase)

IT **9002-13-5**, Urease
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-treatment with catalase; treatment and prevention of Helicobacter infection with C-terminal fragments of recombinant Helicobacter catalase)

IT **336208-58-3 336208-59-4**
RL: BUU (Biological use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; treatment and prevention of Helicobacter infection with C-terminal fragments of recombinant Helicobacter catalase)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 7 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:77363 HCAPLUS
DOCUMENT NUMBER: 135:148063
TITLE: Cloning and characterization of a 22 kDa outer-membrane protein (Omp22) from Helicobacter pylori
AUTHOR(S): Kim, Jang-Seong; Chang, Ji-Hoon; Seo, Won-Young; Yu, Gum-Ju; Chung, Soo-Il; Yum, Jung-Sun
CORPORATE SOURCE: Mogam Biotechnology Research Institute, Yongin, 449-910, S. Korea
SOURCE: Molecules and Cells (2000), 10(6), 633-641
CODEN: MOCEEK; ISSN: 1016-8478
PUBLISHER: Springer-Verlag Singapore Pte. Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Helicobacter pylori is a causative agent of **gastritis** and peptic **ulceration** in humans. As the first step towards development of a **vaccine** against H. pylori infection, we have attempted to identify

protective antigens. A potential target of **vaccine** development would be a H. pylori specific protein, which is surface-exposed and highly antigenic. We identified a 22 kDa outer-membrane protein (Omp22) from H. pylori, which was highly immunoreactive. By screening a H. pylori genomic DNA library with rabbit anti-H. pylori outer-membrane protein antibodies, the omp22 gene was cloned and 1.4 kb of the nucleotide sequence was detd. One open reading frame, encoding a 179-residue polypeptide, was identified and the amino acid sequence deduced showed homol. with peptidoglycan-assocd. lipoproteins. The sequence was conserved among other H. pylori strains. Omp22 protein is expressed as a precursor polypeptide of 179 residues and undergoes lipid modification and cleavage of an 18 amino acid signal peptide to yield a mature protein. Omp22 protein in H. pylori as well as recombinant Omp22 protein expressed in E. coli was localized into the outer membrane and exposed on the cell surface. Omp22 may have the potential as a target antigen for the development of a H. pylori **vaccine**.

IT **352364-15-9**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; cloning and characterization of a 22 kDa outer-membrane protein (Omp22) from Helicobacter pylori)

IT **194675-00-8**, DNA (Helicobacter pylori strain KCTC0217BP gene omp22 plus flanks)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; cloning and characterization of a 22 kDa outer-membrane protein (Omp22) from Helicobacter pylori)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 8 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:70328 HCAPLUS
DOCUMENT NUMBER: 135:179310
TITLE: Evaluation of factors that can affect protective immune responses following oral immunization of recombinant Helicobacter pylori urease apoenzyme
AUTHOR(S): Kim, Jang Song; Chang, Ji Hoon; Park, Eun Jeong; Chung, Soo Il; Yum, Jung Sun
CORPORATE SOURCE: Mogam Biotechnology Research Institute, Kyonggi, 449-910, S. Korea
SOURCE: Journal of Microbiology and Biotechnology (2000), 10(6), 865-872
CODEN: JOMBES; ISSN: 1017-7825
PUBLISHER: Korean Society for Applied Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Helicobacter pylori is the major cause of **gastritis**, peptic **ulcer**, and a principal risk factor for **gastric** cancer. As the first step towards a **vaccine** against H. pylori infection, H. pylori urease was expressed and purified as a recombinant apoenzyme (rUrease) in E. coli. In order to develop an effective immunization protocol using rUrease, the host immune responses were evaluated after the oral immunization of mice with rUrease prepns. plus cholera toxin relative to various conditions, such as the phys. nature of the antigen, the frequency of the booster immunization, the dose of the antigen, and the route of administration. The protective efficacy was assessed using a quant. culture following an H. pylori SS1 challenge. It was demonstrated that rUrease, due to its particulate nature, was more superior than the UreB subunit as a **vaccine** antigen. The oral immunization of rUrease elicited significant systemic and secretory antibody responses,

and activated predominantly Th2-type cellular responses. The bacterial colonization was significantly reduced (.apprx.100-fold) in those mice immunized with three or four weekly oral doses of rUrease plus cholera toxin, when compared to the non-immunized/challenged controls. The protection correlated well with the elicited secretory IgA level against rUrease, and these secretory antibody responses were highly dependent on the frequency of the booster immunization, yet unaffected by the dose of the antigen (25-200 .mu.g). These results demonstrate the remarkable potential of rUrease as a **vaccine** antigen, thereby strengthening the possibility of developing an H. pylori **vaccine** for humans.

IT **9002-13-5**, Urease
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence)
(protective immune responses following oral immunization of recombinant Helicobacter pylori urease apoenzyme)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 9 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:6727 HCAPLUS
DOCUMENT NUMBER: 135:194111
TITLE: Evaluation of immune prophylaxis of recombinant urease subunit of Helicobacter pylori
AUTHOR(S): Shi, Li; Wang, Jide; Chen, Ye; Zhang, Zhenshu; Zhang, Yali; Zhang, Wandai; Zhou, Dianyuan
CORPORATE SOURCE: The Digestive Disease Institute of PLA, Nanfang Hospital, The First Military Medical University, Canton, 510515, Peop. Rep. China
SOURCE: Zhonghua Yixue Zazhi (2000), 80(11), 811-815
CODEN: CHHTAT; ISSN: 0376-2491
PUBLISHER: Zhonghua Yixue Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB The immune prophylaxis of recombinant urease subunit A and B was evaluated. The BALB/C mice were divided into 7 groups: neg. control group, control group with cholera toxin subunit B (CTB), control group with rUreA, control group with rUreB, exptl. group with rUreA + CTB and exptl. group with rUreB + CTB, exptl. group with sonicate + CTB, which were **gastrically** inoculated with 150 mL PBS, 5 .mu.g CTB, 50 .mu.g rUreA, 50 .mu.g rUreB, 50 .mu.g rUreA + CTB and 400 .mu.g sonicate + 5 .mu.g CTB, resp. Two weeks later, the mice were **gastrically** infected with H. pylori (107-108 PCU per time). Four, 8 and 12 wk later, the mice were killed and the immune protection of PBS, CTB, rUreA, rUreB, rUreA + CTB, rUreB + CTB and sonicate + CTB were evaluated by assay of the presence of H.pylori in **gastric** tissue stained with Giemsa by microscopy. The mice in the side-effecting groups of rUreA + CTB and rUreB + CTB were not infected with H.pylori. 12 Wk later, the mice in the 2 groups were killed, and the side effects of rUreA + CTB and rUreB + CTB were evaluated by the infiltration of inflammation cells in **gastric** tissue stained with HE by microscopy. The mice **gastrically** inoculated with CTB, rUreA or rUreB had significantly less H. pylori. The immune protective effect of rUreA, rUreB or sonicate of H. pylori combined with CTB was stronger than that of rUreA, rUreB or sonicate of H. pylori alone. The immune protective effect of rUreA + CTB occurred later than that of rUreB + CTB or sonicate of H.pylori + CTB. The mice immunized with rUreA + CTB, rUreB + CTB or sonicate of H. pylori + CTB were not completely protected from H. pylori infection.

IT **9002-13-5**, Urease
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL

(Biological study); PROC (Process)
(recombinant gene; evaluation of immune prophylaxis of recombinant urease subunit of Helicobacter pylori in mice)

L7 ANSWER 10 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:861846 HCAPLUS
DOCUMENT NUMBER: 134:27474
TITLE: Essential genes of Helicobacter pylori and their gene products and the development of **vaccines** and antibiotics for diagnosis and treatment of infections
INVENTOR(S): Apfel, Heiko; Fuchs, Thilo M.; Gibbs, Carol P.; Hueck, Christoph J.; Meyer, Thomas F.
PATENT ASSIGNEE(S): Max-Planck-Gesellschaft zur Forderung der Wissenschaften e.V., Germany; Creatogen G.m.b.H.
SOURCE: PCT Int. Appl., 376 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000073502	A2	20001207	WO 2000-EP5024	20000531
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
DE 19924965	A1	20001207	DE 1999-19924965	19990531
DE 19927740	A1	20001221	DE 1999-19927740	19990617
DE 19934029	A1	20010125	DE 1999-19934029	19990721

PRIORITY APPLN. INFO.: DE 1999-19924965 A 19990531
DE 1999-19927740 A 19990617
DE 1999-19934029 A 19990721

AB The invention relates to methods for prepg. therapeutic, preventative and/or diagnostic agents for treating microbial infections and to methods for identifying and characterizing essential genes from Helicobacter pylori. The invention also relates to the identified nucleic acids which code for the essential gene products and to the polypeptides which are coded therefrom.

IT **179005-51-7 184050-46-2 184656-26-6**
186468-77-9 193830-72-7 193831-90-2
193831-91-3 193832-07-4 193832-39-2
193832-65-4 193833-80-6 193833-95-3
193834-24-1 193835-88-0 193836-29-2
193836-35-0 193837-28-4 193837-75-1
193837-82-0 193838-20-9 193838-77-6
193838-88-9 193839-00-8 193839-95-1
193840-59-4 193841-35-9 193841-46-2
193841-82-6 193842-22-7 193842-23-8
193843-92-4 193844-38-1 193844-42-7
193844-74-5 193844-77-8 193844-90-5
193844-95-0 193845-41-9 208732-74-5, Protein
GHPO 253 (Helicobacter pylori) **311354-99-1 311355-01-8**
311355-04-1 311355-12-1 311355-14-3

311355-18-7 311355-22-3 311355-26-7
311355-33-6 311355-35-8 311355-39-2
311355-43-8 311355-47-2 311355-58-5
311355-62-1 311355-65-4 311768-65-7
311768-72-6
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; essential genes of Helicobacter pylori and their gene products and development of **vaccines** and antibiotics for diagnosis and treatment of infections)

IT 184050-45-1 184656-25-5 311354-92-4
311354-96-8 311354-97-9 311354-98-0
311355-00-7 311355-02-9 311355-03-0
311355-05-2 311355-06-3 311355-07-4
311355-08-5 311355-09-6 311355-10-9
311355-11-0 311355-13-2 311355-15-4
311355-16-5 311355-17-6 311355-19-8 31135
5-20-1 311355-21-2 311355-23-4
311355-24-5 311355-25-6 311355-27-8
311355-28-9 311355-29-0 311355-30-3
311355-31-4 311355-32-5 311355-34-7
311355-36-9 311355-37-0 311355-38-1
311355-40-5 311355-41-6 311355-42-7
311355-44-9 311355-45-0 311355-46-1
311355-48-3 311355-49-4 311355-50-7
311355-51-8 311355-52-9 311355-53-0
311355-54-1 311355-55-2 311355-56-3
311355-57-4 311355-59-6 311355-60-9
311355-61-0 311355-63-2 311355-64-3
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; essential genes of Helicobacter pylori and their gene products and development of **vaccines** and antibiotics for diagnosis and treatment of infections)

L7 ANSWER 11 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:821256 HCAPLUS
DOCUMENT NUMBER: 134:339313
TITLE: Transgenic plants as a potential source of an oral **vaccine** against Helicobacter pylori
AUTHOR(S): Brodzik, R.; Gaganidze, D.; Henning, J.; Muszynska, G.; Koprowski, H.; Sirko, A.
CORPORATE SOURCE: Institute of Biochemistry and Biophysics, Polish Academy of Sciences, Warsaw, 02-106, Pol.
SOURCE: Progress in Biotechnology (2000), 17(Food Biotechnology), 35-42
CODEN: PBITE3; ISSN: 0921-0423
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Plants are one of several novel hosts that can be used for an inexpensive prodn. of recombinant biopharmaceuticals such as **vaccines**. There is evidence that oral immunization with Helicobacter pylori urease, or its large subunit encoded by the ureB gene in the presence of oral adjuvants, is a feasible strategy for the development of a **vaccine** against this **gastric** pathogen. In this study we report on cloning and expression of the H. pylori ureB gene in a low alkaloid line of tobacco (Nicotiana tabacum cv. LA Burley 21) and in the cells of carrot callus (Daucus carota cv. Dolanka). The evaluation of the UreB level in transgenic tobacco plants and transformed carrot callus was accomplished

and revealed expression levels sufficient for an immunol. study in lab. animals.

IT **9002-13-5**, Urease
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
(gene for H. pylori; Transgenic plants as a potential source of an oral **vaccine** against Helicobacter pylori)

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 12 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:790541 HCAPLUS
DOCUMENT NUMBER: 133:349132
TITLE: Helicobacter pylori antigens for mucosal **vaccination**
INVENTOR(S): Pappo, Jacques
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066624	A1	20001109	WO 2000-SE808	20000428

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: SE 1999-1548 A 19990429

AB The authors disclose the prepn. of a **vaccine** which comprises HpaA and HOP38 polypeptides of H. pylori. Oral immunization with HpaA and HOP38 provided synergistic protection against **gastric** infection.

IT **185858-42-8 185858-47-3 305872-58-6 305872-63-3 305872-65-5 306277-75-8**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; polypeptides of HpaA adhesin and HOP38 protein in relation to **vaccination** against Helicobacter pylori infection)

IT **305872-57-5 305872-59-7 305872-60-0 305872-61-1 305872-62-2 305872-64-4 305872-66-6**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; polypeptides of HpaA adhesin and HOP38 protein in relation to **vaccination** against Helicobacter pylori infection)

IT **169875-77-8**
RL: PRP (Properties)
(unclaimed protein sequence; helicobacter pylori antigens for mucosal **vaccination**)

Searched by Mona Smith

Minnifield 09/955,739

IT **171657-97-9**
RL: PRP (Properties)
(unclaimed sequence; helicobacter pylori antigens for mucosal **vaccination**)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 13 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:668688 HCAPLUS
DOCUMENT NUMBER: 135:14761
TITLE: Quantitative and bioluminescent assay to measure efficacy of conventional and DNA **vaccinations** against Helicobacter pylori
AUTHOR(S): Ozpolat, B.; Rao, X. M.; Osato, M. S.; Graham, D. Y.; Lachman, L. B.
CORPORATE SOURCE: Department of Bioimmunotherapy, University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA
SOURCE: Combinatorial Chemistry and High Throughput Screening (2000), 3(4), 289-302
CODEN: CCHSFU; ISSN: 1386-2073
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Vaccination** against Helicobacter pylori using DNA sequences encoding Urease A and B subunits was compared to immunization with urease antigen and MTP-PE in a liposome formulation. To det. the effectiveness of a **vaccine** against H. pylori in a mouse model it is essential to quantify the no. of H. pylori remaining in the stomachs following challenge with an inoculum of live bacteria. Culture assays and enzymic assays produce inconsistent results often unsuitable to conclude if **vaccine** candidates are protective. To overcome this problem, we developed two assays: (1) a competitive quant. PCR using a colorimetric readout and (2) a non-competitive direct quant. PCR using a highly sensitive bioluminescent readout. The competitive PCR requires coamplification of a segment of the urease C sequence and an internal control std. in a competitive manner using a single set of primers. PCR products were quantified colorimetrically by an ELISA and compared with known quantities of the internal control std. added to the PCR reaction. The highly sensitive, bioluminescent assay measures the amplified DNA directly using a flash-type luminescent tag and a specific probe. The Sydney strain of H. pylori was used for the mouse infection model. Quantification of H. pylori by either the bioluminescent assay or the competitive PCR was reliable, specific and sensitive compared to quant. growth assays which often gave false results. The bioluminescent assay was much more sensitive and less labor/time intensive than the competitive PCR. The bioluminescent assay was able to quantitate as few as 100 bacteria, while the competitive assay could not detect less than 103 bacteria per mouse stomach. Quantification of H. pylori by bioluminescent assay was superior to the competitive assay and may be used for research applications, such as the development of **vaccines**, pathogenesis of **gastric** disease and monitoring of antibiotic treatment.
IT **9002-13-5**, Urease
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(antigen of; quant. and bioluminescent assay to measure efficacy of conventional and DNA **vaccinations** against Helicobacter pylori)
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

Searched by Mona Smith

L7 ANSWER 14 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:351549 HCAPLUS
DOCUMENT NUMBER: 133:16302
TITLE: Protective activity of Helicobacter pylori antigen
INVENTOR(S): Dunkley, Margaret; Harris, Simon
PATENT ASSIGNEE(S): Cortecs (UK) Limited, UK
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029432	A1	20000525	WO 1999-GB3759	19991111
W: CN, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1131346	A1	20010912	EP 1999-954221	19991111
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: GB 1998-25184 A 19981117
WO 1999-GB3759 W 19991111

AB The authors disclose the purifn. and protective activity of HP0310 antigen derived from H. pylori. In one example, mice received HP0310 via intra-Peyer's patch immunization. Immunized mice were protected against subsequent challenge infection with a heterologous strain.

IT **193833-86-2**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; **vaccination** against HP0310 protein of Helicobacter pylori in relation to protection against)

IT **271755-30-7**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; **vaccination** against HP0310 protein of Helicobacter pylori in relation to protection against)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 15 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:282541 HCAPLUS
DOCUMENT NUMBER: 133:41845
TITLE: Immunization with recombinant Helicobacter pylori urease in specific-pathogen-free rhesus monkeys (Macaca mulatta)
AUTHOR(S): Solnick, Jay V.; Canfield, Don R.; Hansen, Lori M.; Torabian, Sima Z.
CORPORATE SOURCE: Departments of Internal Medicine (Division of Infectious Diseases) and Medical Microbiology and Immunology, Davis School of Medicine, University of California, Davis, CA, 95616, USA
SOURCE: Infection and Immunity (2000), 68(5), 2560-2565
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Immunization with urease can protect mice from challenge with Helicobacter pylori, though results vary depending on the particular **vaccine**,

challenge strain, and method of evaluation. Unlike mice, rhesus monkeys are naturally colonized with H. pylori and so may provide a better est. of **vaccine** efficacy in humans. The purpose of this study was to examine the effectiveness of H. pylori urease as a **vaccine** in specific-pathogen (H. pylori)-free rhesus monkeys. Monkeys raised from birth and documented to be free of H. pylori were **vaccinated** with **orogastric** or i.m. urease. Two control monkeys were sham **vaccinated**. All monkeys were challenged with a rhesus monkey-derived strain of H. pylori, and the effects of **vaccination** were evaluated by use of quant. cultures of **gastric** tissue, histol., and measurement of serum IgG and salivary IgA. Despite a humoral immune response, all monkeys were infected after H. pylori challenge, and there were no differences in the d. of colonization. Immunization with urease therefore does not fully protect against challenge with H. pylori. An effective **vaccine** to prevent H. pylori infection will require different or more likely addnl. antigens, as well as improvements in the stimulation of the host immune response.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(immunization with recombinant urease in rhesus monkeys does not prevent infection by Helicobacter pylori)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 16 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:213598 HCAPLUS
DOCUMENT NUMBER: 133:3462
TITLE: Pilot study of phoP/phoQ-deleted Salmonella enterica serovar typhimurium expressing Helicobacter pylori urease in adult volunteers
AUTHOR(S): Angelakopoulos, Haroula; Hohmann, Elizabeth L.
CORPORATE SOURCE: Infectious Disease Division, Department of Medicine, Massachusetts General Hospital, Boston, MA, 02114, USA
SOURCE: Infection and Immunity (2000), 68(4), 2135-2141
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Attenuated Salmonella enterica serovar Typhi has been studied as an oral **vaccine** vector. Despite success with attenuated S. enterica serovar Typhimurium vectors in animals, early clin. trials of S. enterica serovar Typhi expressing heterologous antigens have shown that few subjects have detectable immune responses to vectored antigens. A previous clin. study of phoP/phoQ-deleted S. enterica serovar Typhi expressing Helicobacter pylori urease from a multicopy plasmid showed that none of eight subjects had detectable immune responses to the vectored antigen. To further define the variables important for engendering immune responses to vectored antigens in humans, six volunteers were inoculated with 5.times.107 to 8.times.107 CFU of phoP/phoQ-deleted S. enterica serovar Typhimurium expressing the same antigen. Two of the six volunteers had fever; none had diarrhea, bacteremia, or other serious side effects. The volunteers were more durably colonized than in previous studies of phoP/phoQ-deleted S. enterica serovar Typhi. Five of the six volunteers seroconverted to S. enterica serovar Typhimurium antigens and had strong evidence of anti-Salmonella mucosal immune responses by enzyme-linked immunospot studies. Three of six (three of five who seroconverted to Salmonella) had immune responses in the most sensitive assay of urease-specific Ig prodn. by blood mononuclear cells in vitro. One of these had a fourfold or greater increase in end-point Ig titer in

serum vs. urease. Attenuated S. enterica serovar Typhimurium appears to be more effective than S. enterica serovar Typhi for engendering immune responses to urease. Data suggest that this may be related to a greater stability of antigen-expressing plasmid in S. enterica serovar Typhimurium and/or prolonged intestinal colonization. Specific factors unique to non-typhoidal salmonellae may also be important for stimulation of the **gastrointestinal** immune system.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(humoral immune response to oral immunization with phoP/phoQ-deleted Salmonella typhimurium vector expressing Helicobacter pylori urease)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 17 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:197597 HCAPLUS
DOCUMENT NUMBER: 132:249998
TITLE: Helicobacter pylori membrane antigen and its encoding gene and use as **vaccine**
INVENTOR(S): Murakami, Kazuhisa; Kobayashi, Yoshinao; Wakatsuki, Yoshio
PATENT ASSIGNEE(S): Shionogi Seiyaku K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 18 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000083671	A2	20000328	JP 1998-257343	19980911

AB The gene encoding a 20-kDa Helicobacter pylori membrane antigen is isolated and characterized. The antigen (or protein HPS) can be used for developing diagnostic agents or **vaccine** against the H. pylori-assocd. diseases such as **gastritis** and duodenum **ulcer**.

IT **262347-78-4 262347-79-5**
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; Helicobacter pylori membrane antigen and encoding gene and use as **vaccine**)

IT **207892-87-3 262347-77-3**
RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; Helicobacter pylori membrane antigen and encoding gene and use as **vaccine**)

L7 ANSWER 18 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:183432 HCAPLUS
DOCUMENT NUMBER: 133:130387
TITLE: Quantitation of Helicobacter pylori in the stomach using quantitative polymerase chain reaction assays
AUTHOR(S): Ozpolat, Bulent; Actor, Jeffrey K.; Rao, Xiao-Mei; Lee, Sangjun; Osato, Michael; Graham, David Y.; Lachman, Lawrence B.
CORPORATE SOURCE: Department of Bioimmunotherapy, The University of Texas M. D. Anderson Cancer Center, Houston, TX, 77030, USA

SOURCE: Helicobacter (2000), 5(1), 13-21
CODEN: HELIFL; ISSN: 1083-4389
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background. The d. of Helicobacter pylori is thought to correlate with the degree of inflammation and thus indirectly with the outcome of the infection. Rapid quant. assays of H. pylori in **gastric** or duodenal mucosa are lacking. The aim was to develop quant. assays using the polymerase chain reaction to assess the quantity of H. pylori in the **gastric** mucosa. Methods. Competitive PCR was based on coamplification of a segment of the ureC sequence and an internal control using a single set of primers. PCR products were quantified colorimetrically by an ELISA and compared with known quantities of the internal control std. added to the PCR reaction. The highly sensitive, noncompetitive PCR assay does not use coamplification and measures the amplified DNA sequence using a flash-type luminescent tag and a specific probe. The mouse infected model using H. pylori strain SS-1 was used to develop the assays. Results. Quantification of H. pylori using either the competitive or noncompetitive PCR was reliable, highly sensitive and specific. Conclusions. The ability to rapidly quantitate H. pylori from **gastric** mucosa should be useful to investigate the role of H. pylori d. and infection outcome, as well as to monitor the effectiveness of antibiotic treatment or **vaccines** against H. pylori.

IT **9002-13-5**, Urease
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(**vaccination**; quantitation of Helicobacter pylori in the stomach using quant. polymerase chain reaction assays)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 19 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:81792 HCAPLUS
DOCUMENT NUMBER: 132:221054

TITLE: Identification of immunodominant antigens from Helicobacter pylori and evaluation of their reactivities with sera from patients with different **gastroduodenal** pathologies

AUTHOR(S): Kimmel, Brigitte; Bosserhoff, Armin; Frank, Rainer; Gross, Roy; Goebel, Werner; Beier, Dagmar
CORPORATE SOURCE: Theodor-Boveri-Institut fur Biowissenschaften, Lehrstuhl fur Mikrobiologie, Universitat Wurzburg, Wurzburg, D-97074, Germany

SOURCE: Infection and Immunity (2000), 68(2), 915-920
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Colonization of the **gastric** mucosa by H. pylori is the major cause of **gastroduodenal** pathologies in humans. Studying the outcome of the humoral immune response directed against this **gastric** pathogen may contribute substantially to **vaccine** development and to the improvement of diagnostic techniques based on serol. By using 2-dimensional gel electrophoresis, 29 proteins from H. pylori G27 were identified which strongly react with sera derived from H. pylori-infected patients suffering from different **gastroduodenal** pathologies. These antigens were characterized by mass spectrometry and proved to correspond to products of open reading frames predicted by the H. pylori genome sequence. The comparison of the antigenic patterns

recognized by these sera revealed no assocn. of specific H. pylori antigens with antibodies in patients with particular **gastroduodenal** pathologies.

IT **9002-13-5**, Urease
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(B subunit; immunodominant antigens from Helicobacter pylori and reactivities with sera from patients with different **gastroduodenal** pathol.)

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:68353 HCAPLUS
DOCUMENT NUMBER: 132:127722
TITLE: Urease-based **vaccine** against Helicobacter infection
INVENTOR(S): Park, Jong Beak
PATENT ASSIGNEE(S): Cheil Jedang Corporation, S. Korea
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000003730	A1	20000127	WO 1998-KR216	19980716
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9884643	A1	20000207	AU 1998-84643	19980716

PRIORITY APPLN. INFO.: WO 1998-KR216 A 19980716

AB The present invention relates to a **vaccine** for generating protective immunity against Helicobacter infection in mammals comprising a polyaminoacid prepn. including epitopes exhibited by a Lactobacillus-derived urease in combination with a pharmaceutically acceptable carrier or diluent. The polyaminoacid prepn. comprises a purified Lactobacillus fermentum urease, Lactobacillus reuteri urease or subunits thereof. In addn., the present invention relates to a process for assaying protective immune response in mammals infected with Helicobacter which comprises detg. the presence of antibody reactive with epitopes exhibited by a urease endogenous to said Lactobacillus organism within a sample collected by **gastric** route of said mammals.

IT **9002-13-5**, Urease
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(peptides of; Lactobacillus urease-based **vaccine** against Helicobacter infection)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:717837 HCAPLUS

Minnifield 09/955,739

DOCUMENT NUMBER: 131:314241
TITLE: Stabilized protein crystals, formulations containing them and methods of making them
INVENTOR(S): Margolin, Alexey L.; Khalaf, Nazer K.; St. Clair, Nancy L.; Rakestraw, Scott L.; Shenoy, Bhami C.
PATENT ASSIGNEE(S): Altus Biologics Inc., USA
SOURCE: PCT Int. Appl., 201 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955310	A1	19991104	WO 1999-US9099	19990427
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2330476	AA	19991104	CA 1999-2330476	19990427
AU 9937646	A1	19991116	AU 1999-37646	19990427
EP 1073421	A1	20010207	EP 1999-920064	19990427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002512949	T2	20020508	JP 2000-545510	19990427
US 2002045582	A1	20020418	US 1999-374132	19990810

PRIORITY APPLN. INFO.:

US 1998-83148P	P	19980427
US 1998-224475	A2	19981231
US 1997-70274P	P	19971231
WO 1999-US9099	W	19990427

AB Methods are provided for the stabilization, storage, and delivery of biol. active macromols., such as proteins, peptides and nucleic acids. Methods are provided for the crystn. of proteins and nucleic acids and for the prepn. of stabilized protein or nucleic acid crystals for use in dry or slurry formulations in pharmaceutical and veterinary formulations, diagnostics, cosmetics, food, and agricultural feeds. The crystals are stabilized by addn. of excipients such as carbohydrates or by encapsulating them in a polymeric carrier. Methods are presented for encapsulating proteins, glycoproteins, enzymes, antibodies, hormones, and peptide crystals or crystal formulations into compns. for biol. delivery to humans and animals. Thus, lipase from Candida rugosa was dissolved in distd. water, treated with celite, adjusted to pH 4.8 with AcOH, filtered, ultrafiltered to remove proteins of <30 kDa mol. wt., and crystn. was initiated by addn. of 2-methyl-2,4-pentanediol. Sucrose was added to the mother liquor to a concn. of 10%, and the crystals were sepd. by centrifugation, suspended in EtOH, and air dried at room temp. Alternatively, the lipase crystals were crosslinked and encapsulated in lactic acid/glycolic acid copolymer; the microspheres formed were 90 .mu.m in diam.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(stabilized protein crystals, formulations contg. them and methods of

making them)
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:709918 HCAPLUS
DOCUMENT NUMBER: 132:34431
TITLE: Urease-based mucosal immunization against Helicobacter heilmannii infection induces corpus atrophy in mice
AUTHOR(S): Dieterich, Christine; Bouzourene, Hanifa; Blum, Andre L.; Corthesy-Theulaz, Irene E.
CORPORATE SOURCE: Division of Gastroenterology, Centre Hospitalier Universitaire Vaudois, Lausanne, CH-1011, Switz.
SOURCE: Infection and Immunity (1999), 67(11), 6206-6209
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Mucosal immunization with Helicobacter heilmannii urease B or H. pylori urease, given nasally with cholera toxin, protects BALB/c mice against H. heilmannii infection and reduces a preexisting infection. However, immunization aggravates **gastric** corpus atrophy. The authors' results underline the necessity of defining immunization regimens that do not enhance mucosal damage.
IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(B; urease-based mucosal immunization against Helicobacter heilmannii infection induces corpus atrophy in mice)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:640728 HCAPLUS
DOCUMENT NUMBER: 131:285387
TITLE: A preventive and therapeutic **vaccine** for Helicobacter pylori-associated diseases
INVENTOR(S): Kim, Byung-o; Lee, Byoung-kwang; Yoon, Suk-won; Park, Seung-kook; Yu, Young-hyo; Pyo, Suhkneung; Choi, Deok-joon; Shin, Sung-seup; Jung, Hyung-jin
PATENT ASSIGNEE(S): Daewoong Pharmaceutical Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9949890	A1	19991007	WO 1998-KR72	19980331
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9865247	A1	19991018	AU 1998-65247	19980331

Minnifield 09/955,739

PRIORITY APPLN. INFO.: WO 1998-KR72 19980331

AB The present invention relates to a preventive and therapeutic **vaccine** for H. pylori-assocd. diseases which comprises an active ingredient of a chimeric protein consisting of adhesin, an antigenic protein of H. pylori and A2 and B subunits of Vibrio cholerae toxin as an adjuvant. Since the adhesin/CTXA2B chimeric protein can induce specific antibodies neutralizing H. pylori, it can be used as an active ingredient of diagnostic kit for H. pylori infection and preventive or therapeutic **vaccine** for H. pylori-assocd. diseases as well.

IT **245742-60-3P**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(amino acid sequence; preventive and therapeutic **vaccine** for Helicobacter pylori-assocd. diseases)

IT **245742-59-0P**
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); PROC (Process)
(nucleotide sequence; preventive and therapeutic **vaccine** for Helicobacter pylori-assocd. diseases)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 24 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:554588 HCAPLUS
DOCUMENT NUMBER: 131:307575
TITLE: Isolation of recombinant protective Helicobacter pylori antigens
AUTHOR(S): Hocking, D.; Webb, E.; Radcliff, F.; Rothel, L.; Taylor, S.; Pinczower, G.; Kapouleas, C.; Braley, H.; Lee, A.; Doidge, C.
CORPORATE SOURCE: Research and Development Division, CSL Limited, Parkville, 3052, Australia
SOURCE: Infection and Immunity (1999), 67(9), 4713-4719
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A total of seven clones producing both new and previously described Helicobacter pylori proteins were isolated from a library of H. pylori genomic DNA. The screening approach by which these proteins were detected relied on the use of antisera raised in mice **vaccinated** with Helicobacter felis sonicate plus cholera toxin, a regimen which protects mice from H. pylori challenge. This strategy was designed to maximize the possibility of obtaining antigens which might be capable of conferring protection from H. pylori infection. Two of the clones were shown to encode the urease enzyme and the heat shock protein HspB, which have already been identified as protective antigens. The other five clones were sequenced, protein coding regions were deduced, and these sequences were amplified by PCR for incorporation into Escherichia coli expression vectors. The proteins produced from these expression systems were purified to allow testing for protective efficacy in an H. pylori mouse model. All five proteins were able to facilitate the clearance of a challenge with H. pylori, as judged by an assay of **gastric** urease activity and light microscopy on stomach sections. These results clearly indicate that the screening strategy has successfully identified candidate **vaccine** antigens.

IT **184050-44-0 184050-46-2 184050-48-4**

Searched by Mona Smith

184050-50-8 247164-89-2 247215-98-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; isolation of recombinant protective Helicobacter pylori antigens)

IT **186291-43-0**, GenBank U86607 **186291-44-1**, GenBank U86608
186291-45-2, GenBank U86609 **186291-46-3**, GenBank U86610
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(nucleotide sequence; isolation of recombinant protective Helicobacter pylori antigens)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 25 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:468005 HCAPLUS
DOCUMENT NUMBER: 131:127560
TITLE: Cloning and characterization of the Helicobacter pylori cagI region 5' to the cagA gene and its therapeutic uses
INVENTOR(S): Covacci, Antonello
PATENT ASSIGNEE(S): Chiron S.P.A., Italy
SOURCE: U.S., 252 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5928865	A	19990727	US 1995-477451	19950607
EP 967279	A1	19991229	EP 1999-202698	19930302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 2000333686	A2	20001205	JP 2000-126696	19930302
JP 2000350591	A2	20001219	JP 2000-126695	19930302
US 6090611	A	20000718	US 1995-471491	19950606
WO 9633274	A1	19961024	WO 1996-IB343	19960418
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
AU 9651605	A1	19961107	AU 1996-51605	19960418
EP 821735	A1	19980204	EP 1996-908300	19960418
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11506905	T2	19990622	JP 1996-531592	19960418

PRIORITY APPLN. INFO.:

IT 1992-FI52	A	19920302
US 1995-425194	B2	19950420
US 1995-471491	A2	19950606
WO 1993-EP158	W	19930125
EP 1993-905285	A3	19930302
JP 1993-515309	A	19930302
US 1995-477451	A	19950607
WO 1996-IB343	W	19960418

AB Helicobacter pylori is known to cause or be a cofactor in type B **gastritis**, peptic **ulcers**, and **gastric** tumors.
In both developed and developing countries, a high percentage of people

are infected with this bacterium. The present invention relates generally to a certain Helicobacter pylori region located 5' to the CagA gene locus, to proteins encoded thereby, and to the use of these genes and proteins for diagnostic and **vaccine** applications. This region is present in type I Helicobacter pylori but absent from type II and appears to play a role in virulence.

IT **184491-44-9**, Protein (Helicobacter pylori gene cagA-associated 3174-amino acid) **184539-26-2**, Protein (Helicobacter pylori gene cagA-associated 3177-amino acid) **184539-31-9**, Protein (Helicobacter pylori cagI region 1727-amino acid) **184539-32-0**, Protein (Helicobacter pylori cagI region 1781-amino acid) **184539-33-1**, Protein (Helicobacter pylori cagI region 1720-amino acid) **184539-34-2**, Protein (Helicobacter pylori cagI region 1724-amino acid) **184539-35-3**, Protein (Helicobacter pylori cagI region 1786-amino acid) **184594-41-0**, Protein (Helicobacter pylori cagI region 1732-amino acid) **184594-43-2**, Protein (Helicobacter pylori cagI region 464-amino acid) **184594-44-3**, Protein (Helicobacter pylori cagI region 481-amino acid) **184594-45-4**, Protein (Helicobacter pylori cagI region 471-amino acid) **184594-46-5**, Protein (Helicobacter pylori cagI region 485-amino acid) **184594-47-6**, Protein (Helicobacter pylori cagI region 469-amino acid) **184594-48-7**, Protein (Helicobacter pylori cagI region 462-amino acid) **184594-50-1**, Protein (Helicobacter pylori cagI region 396-amino acid) **184594-51-2**, Protein (Helicobacter pylori cagI region 124-amino acid) **184594-52-3**, Protein (Helicobacter pylori cagI region 382-amino acid) **184594-53-4**, Protein (Helicobacter pylori cagI region 312-amino acid) **184594-54-5**, Protein (Helicobacter pylori cagI region 131-amino acid) **184594-55-6**, Protein (Helicobacter pylori cagI region 136-amino acid) **184594-56-7**, Protein (Helicobacter pylori cagI region 79-amino acid) **184594-57-8**, Protein (Helicobacter pylori cagI region 241-amino acid) **184594-58-9**, Protein (Helicobacter pylori cagI region 131-amino acid) **184594-59-0**, Protein (Helicobacter pylori cagI region 170-amino acid) **184594-61-4**, Protein (Helicobacter pylori cagI region 143-amino acid) **184594-62-5**, Protein (Helicobacter pylori cagI region 159-amino acid) **184594-63-6**, Protein (Helicobacter pylori cagI region 140-amino acid) **184594-64-7**, Protein (Helicobacter pylori cagI region 261-amino acid) **184594-68-1**, Protein (Helicobacter pylori cagI region 122-amino acid) **184594-69-2**, Protein (Helicobacter pylori cagI region 87-amino acid) **184594-70-5**, Protein (Helicobacter pylori cagI region 178-amino acid)
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; cloning and characterization of Helicobacter pylori cagI region 5' to cagA gene and therapeutic uses)

IT **184594-42-1 234436-06-7 234436-07-8 234436-08-9**
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(nucleotide sequence; cloning and characterization of Helicobacter pylori cagI region 5' to cagA gene and therapeutic uses)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 26 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:386468 HCAPLUS
DOCUMENT NUMBER: 131:255783
TITLE: Helicobacter pylori HspA heat-shock protein gene: cloning, expression and immunogenicity

AUTHOR(S): Li, Ming-Feng; Ling, Zhen; Zhang, Ying-Chun; Ma, Ai-Ying
CORPORATE SOURCE: 455 Hospital of PLA, Shanghai, 200052, Peop. Rep. China
SOURCE: Shengwu Huaxue Yu Shengwu Wuli Xuebao (1999), 31(3), 264-268
CODEN: SHWPAU; ISSN: 0582-9879
PUBLISHER: Shanghai Kexue Jishu Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Helicobacter pylori is the causative agent of **gastritis** and peptic **ulcer** in human. The heat-shock protein A(HspA) may stimulate the immunoresponse protecting human body against challenge of H. pylori. The gene encoding the structural A subunit of H. pylori heat-shock protein was amplified from H. pylori chromosomal DNA by PCR, and was inserted in the prokaryotic expression vector pET-22b(+), and then was transformed into the BL-21 (DE3)E. coli strain to express the HspA recombinant protein. HspA gene was measured to be 354 base pairs, and the recombinant protein gene encoded polypeptides of 118 amino acid residues, corresponding to calcd. mol. wt. of 15 kD. Western blot anal. of HspA recombinant protein was confirmed that it could be specifically recognized by the serum of H. pylori-infected patients, and could also be recognized by the serum of immunized Balb/c mice with HspA itself. This result suggests that HspA may be an effective protein **vaccine** for prevention and treatment of the infection of H. pylori.

IT **244756-02-3P**
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; Helicobacter pylori HspA heat-shock protein gene and cloning, expression and immunogenicity)

IT **244756-01-2**
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
(nucleotide sequence; Helicobacter pylori HspA heat-shock protein gene and cloning, expression and immunogenicity)

L7 ANSWER 27 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:234184 HCAPLUS
DOCUMENT NUMBER: 131:72393
TITLE: Immunization with recombinant Helicobacter pylori urease decreases colonization levels following experimental infection of rhesus monkeys
AUTHOR(S): Lee, Cynthia K.; Soike, Kenneth; Hill, Joseph; Georgakopoulos, Kathleen; Tibbitts, Timothy; Ingrassia, Jennifer; Gray, Heather; Boden, James; Kleanthous, Harold; Giannasca, Paul; Ermak, Thomas; Weltzin, Richard; Blanchard, James; Monath, Thomas P.
CORPORATE SOURCE: OraVax, Inc., Cambridge, MA, USA
SOURCE: Vaccine (1999), 17(11-12), 1493-1505
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Rhesus monkeys, naturally colonized with H. pylori as indicated by culture and histol. were immunized with either 40 mg recombinant H. pylori urease administered orally together with 25 .mu.g Escherichia coli heat-labile enterotoxin (LT) or immunized with LT alone. An initial 6 doses were administered over an 8 wk period. All five **vaccinated** monkeys

had a greater than twofold rise in urease-specific serum IgG and IgA level and urease-specific salivary IgA was induced in 3 of 5 **vaccinated** animals after 6 or 7 doses of **vaccine**. **Vaccination** had no measurable therapeutic effect on H. pylori colonization. H. pylori was eradicated from these monkeys with a course of antimicrobials plus omeprazole, a 7th **vaccine** dose was given (10 mo after the 6th dose) and they were rechallenged with H. pylori. Necropsy was performed 23 wk after rechallenge and H. pylori colonization was detd. by histol. examn. of 12 individual **gastric** sites. A significant redn. in colonization (Friedman's anal. of variance) was found in the **vaccinated** animals. Histopathol. examn. of necropsy tissues also revealed a trend towards reduced **gastritis** and epithelial alterations in the **vaccinated** group compared to animals receiving LT alone. This study provides the first evidence for effective **vaccination** of nonhuman primates against H. pylori, and preliminary evidence that a redn. in bacterial d. attributable to immunization may lessen **gastric** inflammation.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(immunization with Helicobacter pylori urease decreases colonization levels following infection of rhesus monkeys)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 28 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:184151 HCAPLUS
DOCUMENT NUMBER: 130:227705
TITLE: Oral **vaccine** comprising Lactobacillus species transformed with **Helicobacter urease**
INVENTOR(S): Tabaqchali, Soad; Wilks, Mark
PATENT ASSIGNEE(S): Queen Mary & Westfield College, UK
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911284	A1	19990311	WO 1998-GB2631	19980902
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9888779	A1	19990322	AU 1998-88779	19980902

PRIORITY APPLN. INFO.: GB 1997-18616 19970902
WO 1998-GB2631 19980902

AB The present invention relates to a **vaccine** comprising a Lactobacillus species that contains a nucleotide sequence that encodes a urease peptide capable of initiating an anti-urease humoral and/or cellular immune response upon administration to a mammalian species. The **vaccine** may be used to treat **gastrointestinal** disorders, such as **gastritis**, that are the result of infection by

Helicobacter strains, for which urease is the most prominent protein component.

IT **9002-13-5**, Urease
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral **vaccine** comprising Lactobacillus species transformed with **Helicobacter urease**)

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 29 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:45201 HCAPLUS
DOCUMENT NUMBER: 130:123818
TITLE: Purified vacuolating toxin from Helicobacter pylori and methods to use antiserums to the antigen
INVENTOR(S): Cover, Timothy L.; Blaser, Martin J.
PATENT ASSIGNEE(S): Vanderbilt University, USA
SOURCE: U.S., 27 pp., Cont.-in-part of U.S. Ser. No. 841,644.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5859219	A	19990112	US 1994-295643	19941027
WO 9316723	A1	19930902	WO 1993-US1558	19930224
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
US 6013463	A	20000111	US 1995-473265	19950607

PRIORITY APPLN. INFO.: US 1992-841644 19920226
WO 1993-US1558 19930224
US 1994-284747 19940802

AB This invention relates to a purified Helicobacter pylori vacuolating toxin and methods to use this toxin to produce protective antibodies against H. pylori infection. Antiserum to this antigen can be used to detect the toxin. Methods to detect anti-toxin antibodies det. the susceptibility of a patient to develop peptic **ulcer** disease, **gastric** carcinoma, or other clin. consequences of H. pylori infection.

IT **219780-40-2P**
RL: BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation)
(nucleotide sequence; purified vacuolating toxin from Helicobacter pylori and methods to use antiserums to the antigen)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 30 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:11297 HCAPLUS
DOCUMENT NUMBER: 130:181197
TITLE: Immunization of mice with urease **vaccine** affords protection against Helicobacter pylori infection in the absence of antibodies and is mediated by MHC class II-restricted responses
AUTHOR(S): Ermak, Thomas H.; Giannasca, Paul J.; Nichols, Richard; Myers, Gwendolyn A.; Nedrud, John; Weltzin, Richard; Lee, Cynthia K.; Kleanthous, Harold; Monath,

Thomas P.
CORPORATE SOURCE: Ora Vax, Inc., Cambridge, MA, 02139, USA
SOURCE: Journal of Experimental Medicine (1998), 188(12), 2277-2288
CODEN: JEMEAV; ISSN: 0022-1007
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We examd. the roles of cell- and antibody-mediated immunity in urease **vaccine**-induced protection against Helicobacter pylori infection. Normal and knockout mice deficient in major histocompatibility complex (MHC) class I, MHC class II, or B cell responses were mucosally immunized with urease plus Escherichia coli heat-labile enterotoxin (LT), or parenterally immunized with urease plus aluminum hydroxide or a glycolipid adjuvant, challenged with H. pylori strain X47-2AL, and H. pylori organisms and leukocyte infiltration in the **gastric** mucosa quantified. In an adjuvant/route study in normal mice, there was a direct correlation between the level of protection and the d. of T cells recruited to the **gastric** mucosa. In knockout studies, oral immunization with urease plus LT protected MHC class I knockout mice [.beta.2-microglobulin (-/-)] but not MHC class II knockout mice [I-Ab (-/-)]. In B cell knockout mice [.mu.MT (-/-)], **vaccine**-induced protection was equiv. to that obsd. in immunized wild-type (+/+) mice; no IgA+ cells were detected in the stomach, but levels of CD4+ cells equiv. to those in the wild-type strain (+/+) were seen. These studies indicate that protection of mice against H. pylori infection by immunization with the urease antigen is dependent on MHC class II-restricted, cell-mediated mechanisms, and antibody responses to urease are not required for protection.

IT **9002-13-5**, Urease
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urease **vaccine** protects mice against Helicobacter pylori infection by MHC class II-restricted and antibody independent responses)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 31 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:684979 HCAPLUS
DOCUMENT NUMBER: 129:286736
TITLE: Recombinant Helicobacter pylori antigen-cholera toxin fusion proteins and their use as H. pylori **vaccines**
INVENTOR(S): Kim, Byung-o; Shin, Sung-seup; Yu, Young-hyo; Park, Myung-hwan; Choi, Dock-joon; Jung, Hyung-jin
PATENT ASSIGNEE(S): Daewoong Pharmaceutical Co., Ltd., S. Korea
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9844130	A1	19981008	WO 1998-KR73	19980331

W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

Searched by Mona Smith

RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

WO 9853082 A1 19981126 WO 1997-KR91 19970521

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9727937	A1	19981211	AU 1997-27937	19970521
AU 9865248	A1	19981022	AU 1998-65248	19980331
US 2001019834	A1	20010906	US 1999-402100	19990927
US 2002045218	A1	20020418	US 2001-760234	20010111

PRIORITY APPLN. INFO.:

KR 1997-11950	A	19970331
KR 1997-11951	A	19970331
WO 1997-KR91	A	19970521
WO 1998-KR73	W	19980331
US 1998-51315	B1	19980403

AB The present invention relates to chimeric proteins consisting of antigenic proteins of Helicobacter pylori and A2 and B subunits of Vibrio cholerae toxin, more specifically, to recombinant DNAs coding for antigenic proteins Helicobacter pylori and A2 and B subunits of Vibrio cholerae toxin, recombinant expression vectors contg. the genes, a process for prepg. the chimeric proteins employing the recombinant microorganisms transformed with the said expression vectors, and preventive and therapeutic **vaccines** comprising the chimeric proteins for Helicobacter pylori-assocd. diseases. The recombinant DNAs which are designed for convenient expression and gene manipulation, can express chimeric proteins having excellent immunogenicity to H. pylori, which are stable in stomach, and penetrate mucous membrane of intestines easily, finally to stimulate prodn. of sIgA. Accordingly, the chimeric proteins expressed from the recombinant DNAs may be used as an active ingredient of a diagnostic kit for H. pylori infection and preventive or therapeutic **vaccine** for H. pylori-assocd. diseases, and may be used in the prodn. of anti-H. pylori antibody.

IT **214276-97-8P 214276-98-9P**

RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amino acid sequence; recombinant Helicobacter pylori antigen-cholera toxin fusion proteins and their use as H. pylori **vaccines**)

IT **214276-92-3 214276-93-4**

RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)

(nucleotide sequence; recombinant Helicobacter pylori antigen-cholera toxin fusion proteins and their use as H. pylori **vaccines**)

L7 ANSWER 32 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1998:629229 HCAPLUS

DOCUMENT NUMBER: 130:79586

TITLE: Development of mouse and rat model of Helicobacter pylori infection

AUTHOR(S): Zeng, Zhirong; Hu, Pinjin; Chen, Minhu; Yu, Fengyan; Chen, Wei; Peng, Xiaozhong

CORPORATE SOURCE: Department of Gastroenterology, First Affiliated Hospital, Sun Yat-sen University of Medical Sciences, Canton, 510080, Peop. Rep. China

SOURCE: Zhonghua Yixue Zazhi (1998), 78(7), 494-497

CODEN: CHHTAT; ISSN: 0376-2491
PUBLISHER: Zhonghua Yixue Zazhi
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB Different rodent models of H. pylori infection were set up to meet different requirement for different purpose of study. Forty two-grade Wistar rats, 40 two-grade C57BL/6 mice and 40 SPF BALB/c mice were randomly divided into two groups: exptl. and control groups. Animals in the exptl. group were inoculated orally Hp strain (Sydney Strain 1, SS1), 0.4 mL of inoculum per mouse, 1.5 mL per rat (109 organisms/mL) 5 times for a week. Five animals in the exptl. and control groups were sacrificed resp. in 4, 8, 12 and 24 wk after the last bacteria inoculum. Histol. and Hp colonization were assessed by HE staining, Gimesa staining, Urease test, and Hp culture. Bacteria were clearly visible at antrum and body in all exptl. animals, but the no. of Hp colonization varied according to the animal strain in 4 wk. Heavy colonization was seen in C57BL/6 in antrum and body, and in BALB/c and Wistar colonization was located mainly at antrum, less at body, which tendered to increase over the expt. time, esp. in Wistar. Hp was neg. in the controls. All animals had no inflammatory changes in 4 wk, however, in 8, 12 and 24 wk in BALB/c, Wistar and C57BL/6 of the exptl. group, mild to moderate chronic active **gastritis** was obsd. in antrum and body, which increased to severity over time. Atrophy **gastritis** was still not seen in 24 wk. SS1 Hp can colonize in the glandular stomach mucosa of BALB/c, C57BL/6 mice and Wistar rats and lead to chronic active **gastritis** in long-term study. SS1 mouse and rat model is adaptable for animal expt. of H. pylori including **vaccine** studies, screening for novel therapeutics and investigation of mechanism of pathogenesis.

IT **9002-13-5**, Urease
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(development of mouse and rat model of Helicobacter pylori infection)

L7 ANSWER 33 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:574857 HCAPLUS
DOCUMENT NUMBER: 129:288856
TITLE: Immunization against natural Helicobacter pylori infection in nonhuman primates
AUTHOR(S): Dubois, Andre; Lee, Cynthia K.; Fiala, Nancy; Kleanthous, Harry; Mehlman, Patrick T.; Monath, Thomas
CORPORATE SOURCE: Laboratory of Gastrointestinal and Liver Studies, Digestive Diseases Division, Department of Medicine, Uniformed Services University of the Health Sciences, , Bethesda, MD, 20814-4799, USA
SOURCE: Infection and Immunity (1998), 66(9), 4340-4346
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Helicobacter pylori infection is widespread in some breeding groups of a rhesus monkey colony (71% H. pylori pos. by 1 yr), and the rate of seroconversion is also high. As a result, these groups can be used to test the safety and efficacy of an anti-H. pylori **vaccine**. Nine-month-old female animals were randomized to receive either 8 mg of recombinant urease (rUre) plus 25 .mu.g of Escherichia coli heat-labile enterotoxin (LT) or placebo plus LT, given four times at 1-wk intervals followed by a booster 1 mo later. Ten months after the start of the immunization, the animals were subjected to endoscopy and biopsy samples were obtained. H. pylori negativity was defined as no H. pylori growth by culture and no H. pylori obsd. at histol. By this criterion, 2 (7%) of 29

animals receiving placebo and 8 (31%) of 26 immunized animals were H. pylori neg. In addn., antral **gastritis** score was significantly less in H. pylori-neg. immunized monkeys than in H. pylori-pos. animals, whether they were given rUre plus LT or placebo plus LT (or, resp.). Interestingly, antral **gastritis** was also significantly less in H. pylori-pos. animals given rUre plus LT than in H. pylori-pos. animals given placebo plus LT. However, quant. cultures did not demonstrate significant differences between the two latter groups. It is concluded that oral administration of rUre **vaccine** plus LT significantly protects nonhuman primates against H. pylori infection while not causing undesirable side effects.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(oral immunization with recombinant urease and enterotoxin protects rhesus monkeys against Helicobacter pylori infection)

L7 ANSWER 34 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:533739 HCAPLUS
DOCUMENT NUMBER: 130:2126
TITLE: Characterization of a Helicobacter pylori **vaccine** candidate by proteome techniques
AUTHOR(S): McAtee, C. Patrick; Young Lim, Moon; Fung, Kevin; Velligan, Mark; Fry, Kirk; Chow, Theresa P.; Berg, Douglas E.
CORPORATE SOURCE: Genelabs Technologies, 505 Penobscot Drive, Redwood City, CA, 94063, USA
SOURCE: Journal of Chromatography, B: Biomedical Sciences and Applications (1998), 714(2), 325-333
CODEN: JCBBEP; ISSN: 0378-4347
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB In a previous two-dimensional (2D) gel electrophoretic study of protein antigens of the **gastric** pathogen, Helicobacter pylori recognized by human sera, one of the highly and consistently reactive antigens, a protein with Mr of approx. 30,000 (Spot 15) seemed to be of special interest because of low yields on N-terminal protein sequencing. This suggested possible N-terminal modification, as the N-terminal sequence anal. of this 30,000 protein (Spot 15) did not provide a definitive match within the H. pylori genomic database. This protein was isolated by 2D polyacrylamide gel electrophoresis, evaluated by liq. chromatog.-mass spectrometry, and found to consist of two related species of approx. 28,100 and 26,500. In parallel, the proteins within this spot were digested in situ with the endoprotease Lys-C. Anal. of the Lys-C digest by matrix-assisted laser desorption time-of-flight mass spectrometry, peptide mapping, and sequence anal. was conducted. Comparison of the mass and sequence of the Lys-C peptides with those derived from a H. pylori genomic library identified an open reading frame of approx. 300 base pairs as the source of the Spot 15 protein. This corresponded to HP0175 in the recently reported H. pylori genome sequence, an open reading frame with some homol. to Campylobacter jejuni cell binding protein 2. Mass spectral and sequence anal. indicated that Spot 15 was a processed product generated by proteolytic cleavage at both the carboxy and amino termini of the 34 open reading frame precursor.

IT **215801-45-9**
RL: PRP (Properties)
(amino acid sequence; characterization of Helicobacter pylori **vaccine** candidate by proteome techniques)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 35 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:377629 HCAPLUS
DOCUMENT NUMBER: 129:160371
TITLE: Systemic immunization with urease protects mice against Helicobacter pylori infection
AUTHOR(S): Guy, Bruno; Hessler, Catherine; Fourage, Sophie; Haensler, Jean; Vialon-Lafay, Elisabeth; Rokbi, Bachra; Millet, Marie-Jose Quentin
CORPORATE SOURCE: Research Department, Marcy l'Etoile, 69280, Fr.
SOURCE: Vaccine (1998), 16(8), 850-856
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of systemic immunization to induce protection against Helicobacter pylori infection has been evaluated in a mouse model. It was obsd. that if appropriate formulations and adjuvants were used such immunization elicited in outbred Swiss mice levels of protection similar or better than those induced by the oral route in the presence of cholera toxin or Escherichia coli heat labile toxin. Recombinant urease mixed with adjuvants, which induced strong Th1 and Th2 responses elicited better protection than urease mixed with adjuvants which induced a predominant Th2 type response only. These expts. demonstrate the feasibility of parenteral immunization against H. pylori and suggest that an appropriate balance between Th1 and Th2 type responses is required to achieve complete protection.
IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(systemic immunization with urease protects mice against Helicobacter pylori infection)

L7 ANSWER 36 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:363199 HCAPLUS
DOCUMENT NUMBER: 129:107724
TITLE: Rectal and intranasal immunizations with recombinant urease induce distinct local and serum immune responses in mice and protect against Helicobacter pylori infection
AUTHOR(S): Kleanthous, Harry; Myers, Gwendolyn A.; Georgakopoulos, Kathleen M.; Tibbitts, Timothy J.; Ingrassia, Jennifer W.; Gray, Heather L.; Ding, Ru; Zhang, Zhen-Zi; Lei, Wende; Nichols, Richard; Lee, Cynthia K.; Ermak, Thomas H.; Monath, Thomas P.
CORPORATE SOURCE: OraVax, Inc., Cambridge, MA, 02139, USA
SOURCE: Infection and Immunity (1998), 66(6), 2879-2886
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To det. the optimal inductive sites for immunization against H. pylori infection, the protective efficacy of recombinant urease (rUre) was assessed for mice given the **vaccine** by either the oral (p.o.), intranasal (i.n.), or rectal route. When mice were immunized with rUre (25 .mu.g p.o. or rectally or 10 .mu.g i.n.) plus heat-labile toxin from Escherichia coli as the mucosal adjuvant, all routes afforded protection against challenge with H. pylori, as indicated by a redn. in

gastric urease activity compared to that of sham-immunized controls. Quant. H. pylori culture of stomach tissue demonstrate a >97% redn. in bacterial burden in mice immunized by all routes. Induction of anti-urease IgA levels in **gastric** luminal secretions after p.o. immunization was greater than after i.n. administration (means, 6.0 and 1.02 ng/mL, resp.) and was dependent upon challenge with H. pylori. However, immunization by the rectal route resulted in the generation of the highest levels of **gastric** anti-urease IgA (mean, 40.89 ng/mL), which was detectable prior to challenge with H. pylori. Immunohistochem. staining of stomach tissue for cells secreting urease-specific antibody and CD4+ T cells showed levels of recruitment to be dependent upon challenge with H. pylori and equiv. for all routes. These results identify both the rectum and nasal passages as suitable inductive sites for urease immunization.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(rectal and intranasal immunizations with recombinant urease induce local and serum immune responses in mice and protect against Helicobacter pylori infection)

L7 ANSWER 37 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:126362 HCAPLUS
DOCUMENT NUMBER: 128:191580
TITLE: Treatment and prevention of Helicobacter infection with recombinant Helicobacter catalase
INVENTOR(S): Doidge, Christopher Vincent; Lee, Adrian; Radcliff, Fiona Jane; Hazell, Stuart Lloyd
PATENT ASSIGNEE(S): CSL Limited, Australia; University of New South Wales
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9806853	A1	19980219	WO 1997-AU515	19970814
W: AU, CA, JP, KR, NZ				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6005090	A	19991221	US 1996-695987	19960815
AU 9737623	A1	19980306	AU 1997-37623	19970814

PRIORITY APPLN. INFO.:
US 1996-695987 19960815
AU 1994-6124 19940608
WO 1995-AU335 19950608
WO 1997-AU515 19970814

AB An antigenic prepn. for use in the treatment or prevention of Helicobacter infection in a mammalian host, comprises recombinant catalase enzyme of Helicobacter bacteria, particularly recombinant catalase enzyme of H. pylori or H. felis, or an immunogenic fragment. Thus, an antigenic prepn. of catalase is used in a **vaccine** compn. for oral administration which includes a mucosal adjuvant such as cholera toxin. Helicobacter catalase may be administered as the sole active immunogen in a **vaccine** compn. or expressed by alive vector. Thus, catalase was purified from H. pylori (clin. strain 921023) and shown to immunize mice against infection by H. pylori or H. felis. E. coli clones expressing catalase from 2 different isolates of H. pylori (isolate RU1 and isolate 921023) were also characterized, and recombinant catalase shown to be an

effective protective antigen for immunization against H. pylori infection.

IT **203528-01-2 203528-02-3**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; treatment and prevention of Helicobacter infection with recombinant Helicobacter catalase)

IT **9002-13-5**, Urease
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(co-treatment with catalase; treatment and prevention of Helicobacter infection with recombinant Helicobacter catalase)

IT **203527-99-5 203528-00-1**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; treatment and prevention of Helicobacter infection with recombinant Helicobacter catalase)

L7 ANSWER 38 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:63897 HCAPLUS
DOCUMENT NUMBER: 128:166039
TITLE: Helicobacter pylori adhesin binding fucosylated histo-blood group antigens revealed by retagging
AUTHOR(S): Ilver, Dag; Arnqvist, Anna; Ogren, Johan; Frick, Inga-Maria; Kersulyte, Dangeruta; Incecik, Engin T.; Berg, Douglas E.; Covacci, Antonello; Engstrand, Lars; Boren, Thomas
CORPORATE SOURCE: Dep. Microbiol., Umea Univ., Umea, SE-901 87, Swed.
SOURCE: Science (Washington, D. C.) (1998), 279(5349), 373-377
CODEN: SCIEAS; ISSN: 0036-8075
PUBLISHER: American Association for the Advancement of Science
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The bacterium Helicobacter pylori is the causative agent for peptic **ulcer** disease. Bacterial adherence to the human **gastric** epithelial lining is mediated by the fucosylated Lewis b (Leb) histo-blood group antigen. The Leb-binding adhesin, BabA, was purified by receptor activity-directed affinity tagging. The bacterial Leb-binding phenotype was assocd. with the presence of the cag pathogenicity island among clin. isolates of H. pylori. A **vaccine** strategy based on the BabA adhesin might serve as a means to target the virulent type I strains of H. pylori.

IT **203011-33-0 203011-34-1**
RL: PRP (Properties)
(amino acid sequence; Helicobacter pylori BabA adhesin binding fucosylated human blood group Leb antigen)

IT **200890-02-4**
RL: PRP (Properties)
(amino acid sequence; Helicobacter pylori BabA and BabB adhesins in binding fucosylated human blood group Leb antigen)

IT **200889-55-0**, GenBank AF001388 **202942-15-2**
RL: PRP (Properties)
(nucleotide sequence; Helicobacter pylori BabA adhesin binding fucosylated human blood group Leb antigen)

IT **202636-15-5**, GenBank AF001389
RL: PRP (Properties)
(nucleotide sequence; Helicobacter pylori BabA and BabB adhesins in binding fucosylated human blood group Leb antigen)

L7 ANSWER 39 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:15772 HCAPLUS
DOCUMENT NUMBER: 128:101086

Minnifield 09/955,739

TITLE: Helicobacter pylori blood group antigen-binding adhesin
INVENTOR(S): Boren, Thomas; Arnqvist, Anna; Normark, Staffan; Ilver, Dag; Hammarstrom, Lennart
PATENT ASSIGNEE(S): Boren, Thomas, Swed.; Arnqvist, Anna; Normark, Staffan; Ilver, Dag; Hammarstrom, Lennart
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9747646	A1	19971218	WO 1997-SE1009	19970610
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2257826	AA	19971218	CA 1997-2257826	19970610
AU 9731999	A1	19980107	AU 1997-31999	19970610
AU 726429	B2	20001109		
EP 909272	A1	19990421	EP 1997-927563	19970610
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001503606	T2	20010321	JP 1998-501515	19970610
US 6410719	B1	20020625	US 1998-21560	19980210

PRIORITY APPLN. INFO.:

SE 1996-2287	A	19960610
SE 1997-1014	A	19970319
US 1997-41040P	P	19970321
WO 1997-SE1009	W	19970610

AB A novel Helicobacter pylori blood group antigen binding (BAB) adhesin protein was isolated and purified, whereby said protein or fractions thereof bind specifically to fucosylated blood group antigens. The protein sequence of said adhesin is disclosed in this application. Simultaneously the DNA sequences for two genes, babA and babB, producing highly similar proteins, are disclosed. Said adhesin and/or DNA is useful for diagnose and therapy and/or prophylaxis directed against H. pylori induced infections, e.g. **gastritis** and acid peptic disease, i.e. active **vaccination**. A new Ig compn., which exhibits specific activity to a Lewisb antigen binding Helicobacter pylori adhesin, or preferably, monoclonal and/or polyclonal antibodies to said adhesin offer a new and more efficient method of treatment and/or prevention of **gastrointestinal** diseases, caused by Helicobacter pylori or other Helicobacter species, i.e. passive **vaccination**.

IT **200890-01-3 200890-02-4**
RL: PRP (Properties)
(amino acid sequence; Helicobacter pylori blood group antigen-binding adhesin and antibody as active and passive **vaccines** in relation to)

IT **200889-55-0 200889-56-1**
RL: PRP (Properties)
(nucleotide sequence; Helicobacter pylori blood group antigen-binding adhesin and antibody as active and passive **vaccines** in relation to)

Searched by Mona Smith

L7 ANSWER 40 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:772606 HCAPLUS
DOCUMENT NUMBER: 128:58307
TITLE: Induced by Contact with Epithelium gene iceA of Helicobacter pylori, diagnosis of H. pylori infection, and treatment and prevention of peptic **ulcers**
INVENTOR(S): Miller, Geraldine G.; Peek, Richard M., Jr.; Thompson, Stuart A.; Blaser, Martin J.
PATENT ASSIGNEE(S): Vanderbilt University, USA; Miller, Geraldine G.; Peek, Richard M., Jr.; Thompson, Stuart A.; Blaser, Martin J.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9743901	A1	19971127	WO 1997-US8558	19970520
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5780278	A	19980714	US 1996-650528	19960520
CA 2227171	AA	19971127	CA 1997-2227171	19970520
AU 9730733	A1	19971209	AU 1997-30733	19970520
AU 736089	B2	20010726		
EP 861027	A1	19980902	EP 1997-925659	19970520
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 11511032	T2	19990928	JP 1997-542660	19970520
US 6004354	A	19991221	US 1998-60584	19980415
US 6107464	A	20000822	US 1999-413140	19991006

PRIORITY APPLN. INFO.: US 1996-650528 A2 19960520
WO 1997-US8558 W 19970520
US 1998-60584 A3 19980415

AB A purified IceA protein of Helicobacter pylori is provided. The protein is expressed as either an IceA 1 or an IceA 2 variant. A purified polypeptide fragment of the IceA protein is also provided. An antigenic fragment of IceA is provided. An isolated nucleic acid that encodes an IceA protein of H. pylori is provided. A nucleic acid that encodes an IceA 1 variant and a nucleic acid that encodes an IceA 2 variant is also provided. Fragments of the IceA gene are provided. A method of detecting the presence of an antibody against H. pylori in a sample is provided. The method comprises the following steps: a) contacting the sample with a purified IceA protein of H. pylori or a H. pylori-specific fragment thereof; and b) detecting the binding of the antibody in the sample to the protein or fragment, the detection of biding indicating the presence in the sample of antibodies against H. pylori. A method of detecting the presence of an antibody against an **ulcerative** H. pylori strain in a sample is also provided. The reported expts. demonstrate that adherence of H. pylori to **gastric** epithelial cells induces strain-specific expression of a novel **ulcer**-assocd. gene, iceA, which exists in two major allelic variants. The increased expression of iceA following adherence and its assocn. with peptic **ulcer** disease suggest it may play a role in detg. increased virulence.

IT **200296-20-4 200296-21-5 200298-65-3**
200358-91-4
RL: PRP (Properties)

(amino acid sequence; induced by Contact with Epithelium gene iceA of Helicobacter pylori, diagnosis of H. pylori infection, and treatment and prevention of peptic **ulcers**)

IT **200298-64-2 200298-66-4 200298-67-5 200298-68-6 200298-69-7 200298-70-0 200298-71-1 200298-72-2 200298-73-3**, DNA (Helicobacter pylori gene iceA) **200298-74-4**
RL: PRP (Properties)
(nucleotide sequence; induced by Contact with Epithelium gene iceA of Helicobacter pylori, diagnosis of H. pylori infection, and treatment and prevention of peptic **ulcers**)

L7 ANSWER 41 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:677623 HCAPLUS
DOCUMENT NUMBER: 127:330049
TITLE: **Gastritis** in urease-immunized mice after Helicobacter felis challenge may be due to residual bacteria
AUTHOR(S): Ermak, Thomas H.; Ding, Ru; Ekstein, Bruce; Hill, Joseph; Myers, Gwendolyn A.; Lee, Cynthia K.; Pappo, Jacques; Kleanthous, Harold K.; Monath, Thomas P.
CORPORATE SOURCE: OraVax, Inc., Cambridge, MA, USA
SOURCE: Gastroenterology (1997), 113(4), 1118-1128
CODEN: GASTAB; ISSN: 0016-5085
PUBLISHER: Saunders
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Oral Immunization with recombinant Helicobacter pylori urease (rUre) coadministered with a mucosal adjuvant protects mice against challenge with Helicobacter felis. In this study, the duration of protection and **gastritis** after challenge were characterized at sequential time intervals up to 1 yr. Outbred Swiss-Webster mice were orally immunized with rUre plus adjuvant and examd. for the presence of H. felis infection and leukocyte infiltration into the **gastric** mucosa. When defined by **gastric** urease activity, 70%-95% of rUre-immunized mice were protected for between 2 and 57 wk. Challenge with H. felis increased the inflammatory response in the **gastric** mucosa of rUre-immunized mice, which also had elevated CD4+ and CD8+ T cells. The CD8+ cells represented a population of **gastric** intraepithelial cells, which expressed the mucosal .alpha.E-integrin. Epithelial changes consisting of parietal cell loss and hyperplasia of the epithelium occurred in approx. 20% of the mice. Antimicrobial triple therapy significantly decreased the degree of **gastritis** and epithelial alteration in the stomach. These results indicate that oral immunization of mice with rUre produces a long-lasting inhibition of H. felis infection but that residual bacteria may produce a persistent lymphocytic infiltration under these exptl. conditions.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(of Helicobacter pylori; **gastritis** in urease-immunized mice after Helicobacter felis challenge may be due to residual bacteria)

L7 ANSWER 42 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:655716 HCAPLUS
DOCUMENT NUMBER: 127:327220
TITLE: Characterization of Helicobacter pylori dapE and construction of a conditionally lethal dapE mutant
AUTHOR(S): Karita, Mikio; Etterbeek, Michele L.; Forsyth, Mark

H.; Tummuru, Murali K. R.; Blaser, Martin J.
CORPORATE SOURCE: Division of Infectious diseases, Department of Medicine, Vanderbilt University School of Medicine, Nashville, TN, 37232-2605, USA
SOURCE: Infection and Immunity (1997), 65(10), 4158-4164
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Helicobacter pylori colonizes the human **gastric** mucosa and causes **gastritis, ulceration,** or **gastric** cancer. A previously uncharacterized region of the H. pylori genome was identified and sequenced. This region includes a putative operon contg. three open reading frames termed gidA (1,866 bp), dapE (1,167 bp), and orf2 (753 bp); the gidA and dapE products are highly homologous to other bacterial proteins. In E. coli, dapE encodes N-succinyl-L-diaminopimelic acid desuccinylase, which catalyzes the hydrolysis of N-succinyl-L-diaminopimelic acid to L-diaminopimelic acid (L-DAP) and succinate. When wild-type H. pylori strains were transformed to selected for dapE mutagenesis, mutants were present when plates were supplemented with DAP but not with lysine; orf2 mutants were selected without DAP supplementation. Consistent with the finding that GidA is essential in Escherichia coli, the authors were unable to obtain a gidA mutant in H. pylori despite evidence that insertional mutagenesis had occurred. The position of gidA, dapE, and orf2 suggest that they form an operon, which was supported by slot blot RNA hybridization and reverse transcriptase PCR studies. The data imply that the H. pylori dapE mutant may be useful as a conditionally lethal **vaccine.**

IT **197983-20-3 197983-21-4 197983-22-5**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; characterization of Helicobacter pylori dapE and construction of conditionally lethal dapE mutant)

IT **194517-34-5**, GenBank AF008565
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(characterization of Helicobacter pylori dapE and construction of conditionally lethal dapE mutant)

L7 ANSWER 43 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:506615 HCAPLUS
DOCUMENT NUMBER: 127:146507
TITLE: Helicobacter pylori oxidoreductase enzymes and their uses
INVENTOR(S): Chalk, Peter Andrew; Clayton, Christopher Leeson; Kelly, David Jacob; Hughes, Nicola Jane
PATENT ASSIGNEE(S): Glaxo Group Limited, UK; Chalk, Peter Andrew; Clayton, Christopher Leeson; Kelly, David Jacob; Hughes, Nicola Jane
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9723626	A1	19970703	WO 1996-GB3119	19961217

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,

DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9711854 A1 19970717 AU 1997-11854 19961217
PRIORITY APPLN. INFO.: GB 1995-26407 19951222
WO 1996-GB3119 19961217

AB Oxidoreductase enzymes have been identified in H. pylori and can be used to screen for agents effective against H. pylori-mediated diseases or disorders such as **gastritis** and **ulcers**. The preferred oxidoreductase enzymes are 2-oxoglutarate:ferredoxin oxidoreductase and pyruvate:flavodoxin oxidoreductase. These enzymes (and their constituent subunits) or derivs. or homologs of them can be used in pharmaceutical compns. or used as antibody Fab and Fv fragments to develop **vaccines** to H. pylori. The anti-H. pylori antibodies can be either monoclonal or polyclonal. Sequences of the genes and the corresponding proteins for both 4-subunit oxidoreductase enzymes were detd. Oxidoreductase inhibitors specific for the two claimed H. pylori enzymes can also be used as therapeutic agents.

IT **193226-92-5P**
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(2-oxoglutarate (Helicobacter pylori OorC subunit)amino acid sequence; isolation, structure, and activity of Helicobacter pylori oxidoreductase enzymes and their use in screening for anti-H. pylori agents)

IT **193226-89-0P 193226-90-3P 193226-91-4P**
193226-94-7P 193226-95-8P 193226-96-9P
193226-97-0P
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; isolation, structure, and activity of Helicobacter pylori oxidoreductase enzymes and their use in screening for anti-H. pylori agents)

IT **193226-88-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(nucleotide sequence; isolation, structure, and activity of Helicobacter pylori oxidoreductase enzymes and their use in screening for anti-H. pylori agents)

IT **193226-93-6P**
RL: PRP (Properties); PUR (Purification or recovery); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; isolation, structure, and activity of Helicobacter pylori oxidoreductase enzymes and their use in screening for anti-H. pylori agents)

L7 ANSWER 44 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:347305 HCAPLUS
DOCUMENT NUMBER: 127:16332
TITLE: Studies on the outer membrane proteins of Helicobacter pylori as the **vaccine** antigens for oral administration
AUTHOR(S): Park, Hyung-Bae; Choe, Tae-Boo
CORPORATE SOURCE: Department of Microbiological Engineering, Konkuk University, Seoul, 143-701, S. Korea

SOURCE: Sanop Misaengmul Hakhoechi (1997), 25(2), 129-136
CODEN: SMHAEH; ISSN: 0257-2389
PUBLISHER: Korean Society for Applied Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: Korean

AB H. pylori is a spiral-shaped, microaerophilic human **gastric** pathogen causing chronic-active **gastritis** in assocn. with duodenal **ulcer** and **gastric** cancer. To investigate the possibility of H. pylori outer membrane proteins (OMPs) as the oral **vaccine** antigens, sarcosine-insol. outer membrane fraction was prepd. from H. pylori NCTC 11637. The major OMPs having apparent mol. masses of 62 kDa, 54 kDa, and 33 kDa were detected by SDS-PAGE, and were identified as urease B subunit (UreB), heat shock protein (Hsp54 kDa), and urease A subunit (UreA), resp. Minor protein bands of 57 kDa, 52 kDa, 40 kDa, 36 kDa, and 31 kDa were also obsd. The antigenicity of H. pylori OMPs and antigenic cross-reactivity among the strains were detd. by immunoblot anal. using anti-H. pylori OMPs antisera or intestinal lavage solns. The results showed that UreB, Hsp54 kDa, UreA, and 40 kDa proteins vigorously stimulated mucosal immune response rather than systemic immunity. These proteins thus seem to be useful as candidates for the oral **vaccine**. The immunoblotting results with surface proteins from 8 isolated H. pylori strains were similar to that of H. pylori NCTC 11637. The IgA which arose from oral administration of H. pylori OMPs, was able to bind H. pylori whole-cells.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A and B subunits; outer membrane proteins of Helicobacter pylori as **vaccine** antigens for oral administration)

L7 ANSWER 45 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:229088 HCAPLUS
DOCUMENT NUMBER: 126:303498
TITLE: Localization of Helicobacter pylori urease and heat shock protein in human **gastric** biopsies
AUTHOR(S): Dunn, Bruce E.; Vakil, Nimish B.; Schneider, Barbara G.; Miller, Margaret M.; Zitzer, Jason B.; Peutz, Thomas; Phadnis, Suhas H.
CORPORATE SOURCE: Department of Pathology, Medical College of Wisconsin, Milwaukee, WI, 53295-1000, USA
SOURCE: Infection and Immunity (1997), 65(4), 1181-1188
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Helicobacter pylori is a spiral, gram-neg. bacterium which causes chronic **gastritis** and plays a crit. role in peptic **ulcer** disease, **gastric** carcinoma, and **gastric** **lymphoma**. H. pylori expresses significant urease activity which is an essential virulence factor. Since a significant fraction of urease activity is located on the surface of the bacterium, the urease mol. is a logical choice as an antigen for a **vaccine**; currently recombinant urease apoenzyme is being tested as a **vaccine** in phase II clin. trials. The authors have recently demonstrated that urease and HspB (a homolog of the GroEL heat shock protein) become assocd. with the surface of H. pylori in vitro in a novel manner: these cytoplasmic proteins are released by bacterial autolysis and become adsorbed to the surface of intact bacteria, reflecting the unique characteristics of the outer membrane. To det. if similar mechanisms are operative in vivo, the

authors detd. the ultrastructural locations of urease and HspB within bacteria present in human **gastric** biopsies. The results demonstrate that both urease and HspB are located within the cytoplasm of all bacteria examd. in human **gastric** biopsies. Interestingly, a significant proportion of the bacteria examd. also possessed variable amts. of surface-assocd. urease and HspB antigen (from 5-50% of the total antigenic material), indicating that in vivo, H. pylori has surface characteristics which enable it to adsorb cytoplasmic proteins. This is consistent with an altruistic autolysis model in which H. pylori uses genetically programmed bacterial autolysis to release urease and other cytoplasmic proteins which are subsequently adsorbed onto the surface of neighboring viable bacteria. These observations have important implications regarding pathogenesis and development of **vaccines** for H. pylori.

IT **9002-13-5**, Urease
RL: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(Helicobacter pylori urease and HspB protein localization in human stomach)

L7 ANSWER 46 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:124447 HCAPLUS
DOCUMENT NUMBER: 126:130583
TITLE: Compositions containing antigen and lipoprotein and adjuvant for inducing immunological response in host
INVENTOR(S): Becker, Robert S.; Huebner, Robert C.; Gray, Maryann B.; Biscardi, Karen S.; Erdile, Lorne F.; Guy, Bruno
PATENT ASSIGNEE(S): Connaught Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9640290	A1	19961219	WO 1996-US8866	19960605
W: AU, CA, FI, JP, NO				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6251405	B1	20010626	US 1995-476656	19950607
US 6379675	B1	20020430	US 1996-588621	19960119
AU 9661519	A1	19961230	AU 1996-61519	19960605
AU 717890	B2	20000406		
EP 831937	A1	19980401	EP 1996-919085	19960605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11510370	T2	19990914	JP 1996-501336	19960605
NO 9705620	A	19980204	NO 1997-5620	19971204
FI 9704423	A	19980204	FI 1997-4423	19971205

PRIORITY APPLN. INFO.:
US 1995-476656 A 19950607
US 1996-588621 A 19960119
WO 1996-US8866 W 19960605

AB **Vaccine** compns. contg. at least one antigen and at least one lipoprotein and optionally an adjuvant is disclosed. The lipoprotein can itself be antigenic or immunogenic. The antigen can be influenza hemagglutinin (HA) and the lipoprotein a recombinantly expressed product having an OspA leader for lipidation and PspA for the protein portion. The antigen can also be OspC and the lipoprotein OspA.

IT **9002-13-5**, Urease

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antigen; compns. contg. antigen and lipoprotein and adjuvant for inducing immunol. response in host)

L7 ANSWER 47 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:210 HCAPLUS
DOCUMENT NUMBER: 126:29069
TITLE: Cloning and characterization of the Helicobacter pylori cagI region 5' to the cagA gene and its therapeutic uses
INVENTOR(S): Covacci, Antonello
PATENT ASSIGNEE(S): Biocine S.P.A., Italy
SOURCE: PCT Int. Appl., 305 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633274	A1	19961024	WO 1996-IB343	19960418
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
US 5928865	A	19990727	US 1995-477451	19950607
AU 9651605	A1	19961107	AU 1996-51605	19960418
EP 821735	A1	19980204	EP 1996-908300	19960418
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11506905	T2	19990622	JP 1996-531592	19960418

PRIORITY APPLN. INFO.:
US 1995-425194 A 19950420
US 1995-477451 A 19950607
IT 1992-FI52 A 19920302
US 1995-471491 A2 19950606
WO 1996-IB343 W 19960418

AB Helicobacter pylori is known to cause or be a cofactor in type B **gastritis**, peptic **ulcers**, and **gastric** tumors. In both developed and developing countries, a high percentage of people are infected with this bacterium. The present invention relates generally to a certain H. pylori region located 5' to the CagA gene locus, to proteins encoded thereby, and to the use of these genes and proteins for diagnostic and **vaccine** applications. This region is present in type I H. pylori but absent from type II and appears to play a role in virulence.

IT **184491-43-8**, Protein (Helicobacter pylori gene cagA)
184491-44-9 184539-26-2
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; cloning and characterization of Helicobacter pylori cagI region 5' to cagA gene and its therapeutic uses)

IT **184539-25-1 184539-27-3 184539-28-4**
184539-29-5 184539-30-8 184539-31-9
184539-32-0 184539-33-1 184539-34-2
184539-35-3 184594-41-0 184594-42-1
184594-43-2 184594-44-3 184594-45-4
184594-46-5 184594-47-6 184594-48-7

184594-49-8 184594-50-1 184594-51-2
184594-52-3 184594-53-4 184594-54-5
184594-55-6 184594-56-7 184594-57-8
184594-58-9 184594-59-0 184594-60-3
184594-61-4 184594-62-5 184594-63-6
184594-64-7 184594-65-8 184594-66-9
184594-67-0 184594-68-1 184594-69-2
184594-70-5
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cloning and characterization of Helicobacter pylori cagI region 5' to cagA gene and its therapeutic uses)

L7 ANSWER 48 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:740354 HCAPLUS
DOCUMENT NUMBER: 126:6446
TITLE: Protective Helicobacter antigens
INVENTOR(S): Doidge, Christopher Vincent; Lee, Adrian; Radcliff, Fiona Jane; Hocking, Dianna Margaret; Webb, Elizabeth Ann
PATENT ASSIGNEE(S): Csl Ltd., Australia
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9633220	A1	19961024	WO 1996-AU225	19960419
W: AU, CA, JP, KR, NZ, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2217496	AA	19961024	CA 1996-2217496	19960419
AU 9652621	A1	19961107	AU 1996-52621	19960419
AU 693679	B2	19980702		
ZA 9603133	A	19970709	ZA 1996-3133	19960419
EP 821698	A1	19980204	EP 1996-908930	19960419
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11504206	T2	19990420	JP 1996-531353	19960419

PRIORITY APPLN. INFO.:
AU 1995-2575 A 19950421
AU 1995-3931 A 19950703
AU 1996-7565 A 19960116
WO 1996-AU225 W 19960419

AB Protective Helicobacter antigens, esp. H. pylori antigens, and the use of these antigens as **vaccines** for the treatment or prevention of **gastroduodenal** disease assocd. with H. pylori infection. Mol. cloning of H. pylori antigens or proteins was performed, and recombinant H. pylori antigens (i.e. 13, 17, 19, 29, 36 and 50 kDa) were cloned. subcloned, expressed, purified, and tested in mouse model.

IT **9002-13-5**, Urease
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Helicobacter; recombinant Helicobacter pylori or felis antigens as **vaccine** for **gastroduodenal** disease)

IT **184050-44-0 184050-46-2 184050-48-4**
184050-50-8 184050-51-9
RL: PRP (Properties)
(amino acid sequence; cDNA sequences for Helicobacter pylori antigens

in relation to **vaccine** for **gastroduodenal** disease)

IT **184050-43-9 184050-45-1 184050-47-3**
184050-49-5 184050-56-4
RL: PRP (Properties)
(nucleotide sequence; cDNA sequences for Helicobacter pylori antigens in relation to **vaccine** for **gastroduodenal** disease)

L7 ANSWER 49 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:731124 HCAPLUS
DOCUMENT NUMBER: 126:70729
TITLE: Immunomagnetic bead enrichment and PCR for detection of Helicobacter pylori in human stools
AUTHOR(S): Nilsson, Hans-Olof; Aleljung, Paer; Nilsson, Ingrid; Tyszkiewicz, Tadeusz; Wadstroem, Torkel
CORPORATE SOURCE: Department of Medical Microbiology, University of Lund, Soelvegatan 23, S-223 62, Lund, Swed.
SOURCE: Journal of Microbiological Methods (1996), 27(1), 73-79
CODEN: JMIMDQ; ISSN: 0167-7012
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB An immunomagnetic bead-based polymerase chain reaction assay (IMS-PCR) was developed for the detection of Helicobacter pylori in exptl. inoculated human stools and human clin. stool samples. Magnetic beads coated with anti-H. pylori rabbit antibodies were used for enrichment and concn. of H. pylori from fecal samples. Taq polymerase inhibitors, found in human feces, are efficiently removed by the immunomagnetic sepn. (IMS) and subsequent washing of the magnetic beads. Conditions of the assay were developed and optimized with feces from a healthy, H. pylori seroneg., individual. Feces was inoculated with serial dilns. of either the spiral or the coccoid form of H. pylori. These 2 morphol. forms could be detected at similar concns. when inoculated in feces using an optimized IMS-PCR method. In 1 g of feces less than 2.5 .times. 104 H. pylori cells were detected as measured with 2 sep. sets of PCR-primers, based on a urease A subunit gene sequence and a gene sequence encoding a 26-kDa surface protein of H. pylori. Previously, no report has shown a sensitivity below 106 H. pylori in feces PCR. Preliminary anal. of stool samples from 17 patients with symptoms of **gastritis** and esophagitis by IMS-PCR showed a good correlation with EIA-anal. of H. pylori serum-antibodies from these patients. The results indicate that H. pylori cells are shed in feces of infected patients and that immunomagnetic bead PCR might be an appropriate method for clin. diagnosis and studies involving immunoprophylaxis, antibiotic treatment, as well as **vaccine** candidates.

IT **9002-13-5**, Urease
RL: MSC (Miscellaneous)
(A, PCR primers based on gene for; immunomagnetic bead enrichment and PCR for detection of Helicobacter pylori in human stools)

L7 ANSWER 50 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:121144 HCAPLUS
DOCUMENT NUMBER: 124:168822
TITLE: Helicobacter pylori nickel-binding protein sequence, gene, and potential use in **vaccination**, **ulcer** or cancer therapy, and environmental nickel removal
INVENTOR(S): Plaut, Andrew G.; Gilbert-Rothstein, Joanne V.; Wright, Andrew
PATENT ASSIGNEE(S): New England Medical Center Hospitals, Inc., USA;

Minnifield 09/955,739

	Trustees of Tufts College
SOURCE:	PCT Int. Appl., 32 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9533767	A1	19951214	WO 1995-US5772	19950509
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5780040	A	19980714	US 1994-255457	19940608
CA 2192312	AA	19951214	CA 1995-2192312	19950509
EP 770092	A1	19970502	EP 1995-919083	19950509
R: AT, CH, DE, FR, GB, LI				
JP 10506521	T2	19980630	JP 1995-500888	19950509
US 5972348	A	19991026	US 1998-115032	19980714

PRIORITY APPLN. INFO.:	US 1994-255457	19940608
	WO 1995-US5772	19950509

AB The application discloses a nickel-binding protein and its encoding DNA isolated from Helicobacter pylori. This organism is the primary cause of chronic **gastritis** and ensuing peptic **ulcers**, and has been implicated in stomach cancer. The nickel-binding protein is useful to inhibit assembly of active ureases, the enzymes responsible for the pathogenic features of the bacterium. Potential uses include as a **vaccine** a diagnostic, a drug target, and a therapy in itself.

IT **169149-23-9**
RL: ANT (Analyte); NUU (Other use, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; Helicobacter pylori nickel-binding protein sequence, gene, and potential use in **vaccination**, **ulcer** or cancer therapy, and environmental nickel removal)

IT **9002-13-5**, Urease
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(nickel-dependent subunit assembly inhibition; Helicobacter pylori nickel-binding protein sequence, gene, and potential use in **vaccination**, **ulcer** or cancer therapy, and environmental nickel removal)

IT **173763-86-5**
RL: NUU (Other use, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence of; Helicobacter pylori nickel-binding protein sequence, gene, and potential use in **vaccination**, **ulcer** or cancer therapy, and environmental nickel removal)

L7 ANSWER 51 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1995:913485 HCAPLUS
DOCUMENT NUMBER:	123:312246
TITLE:	Helicobacter pylori vacuolating toxin gene product useful for immunization
INVENTOR(S):	Cover, Timothy L.; Blaser, Martin J.
PATENT ASSIGNEE(S):	Vanderbilt Univ., USA
SOURCE:	PCT Int. Appl., 63 pp.
	CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9522988	A1	19950831	WO 1995-US2219	19950223
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5721349	A	19980224	US 1994-200232	19940223
AU 9519274	A1	19950911	AU 1995-19274	19950223
EP 749322	A1	19961227	EP 1995-911868	19950223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09512703	T2	19971222	JP 1995-522437	19950223
PRIORITY APPLN. INFO.:			US 1994-200232	19940223
			US 1992-841644	19920226
			WO 1995-US2219	19950223

AB Helicobacter pylori is the major causative agent of chronic superficial **gastritis** in humans and is assocd. with the pathogenesis of peptic **ulcer** disease and possibly **gastric** cancer. The Helicobacter pylori vacuolating toxin gene was cloned and sequenced and the protein purified. An immunogenic amt. of a protein in a pharmaceutically acceptable carrier is described providing immunization against H. pylori infection. In addn., nucleic acids that selectively hybridize with the vacuolating toxin encoding gene are described for identification. Lastly, a genetically altered mutant strain of H. pylori that does not express a functional vacuolating toxin is presented.

IT **155981-96-7P 155981-97-8P**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; helicobacter pylori vacuolating toxin gene product useful for immunization)

IT **154681-04-6P 170213-64-6P**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(nucleotide sequence; helicobacter pylori vacuolating toxin gene product useful for immunization)

L7 ANSWER 52 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:852008 HCAPLUS
DOCUMENT NUMBER: 123:237791
TITLE: Urease-based **vaccine** and treatment for Helicobacter infection
INVENTOR(S): Michetti, Pierre; Corthesy-Theulaz, Irene; Blum, Andre; Davin, Catherine; Haas, Rainer; Kraehenbuhl, Jean-Pierre; Saraga, Emilia
PATENT ASSIGNEE(S): Oravax, Inc., USA
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9522987	A1	19950831	WO 1995-US2202	19950223

W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TT, UA
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

US 6290962	B1	20010918	US 1994-200346	19940223
AU 9519681	A1	19950911	AU 1995-19681	19950223
AU 694195	B2	19980716		
EP 751786	A1	19970108	EP 1995-912583	19950223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
BR 9506884	A	19970819	BR 1995-6884	19950223
JP 09509661	T2	19970930	JP 1995-522429	19950223
PL 179149	B1	20000731	PL 1995-316007	19950223
NO 9603508	A	19961021	NO 1996-3508	19960822
FI 9603281	A	19961022	FI 1996-3281	19960822

PRIORITY APPLN. INFO.:

US 1994-200346	A	19940223
US 1992-970996	B2	19921103
US 1993-85938	A2	19930706
WO 1995-US2202	W	19950223

AB A method of eliciting in a mammalian host a protective immune response to Helicobacter infection and treatment of Helicobacter infection by administering to the host an immunogenically effective amt. of a **Helicobacter urease** or urease subunits as antigen is described. **Vaccine** compns. are also provided.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(urease-based **vaccine** and treatment for Helicobacter infection)

L7 ANSWER 53 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:772761 HCAPLUS
DOCUMENT NUMBER: 123:167618
TITLE: Immunogenic compositions against Helicobacter infection, polypeptides for use in the compositions and nucleic acid sequences encoding said polypeptides
INVENTOR(S): Labigne, Agnes; Suerbaum, Sebastien; Ferrero, Richard
PATENT ASSIGNEE(S): Institut Pasteur, Fr.; Institut National de la Sante et de la Recherche Medicale (INSERM)
SOURCE: PCT Int. Appl., 127 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9514093	A1	19950526	WO 1993-EP3259	19931119
W: JP				
CA 2144307	AA	19941124	CA 1994-2144307	19940519
WO 9426901	A1	19941124	WO 1994-EP1625	19940519
W: AU, CA, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9469290	A1	19941212	AU 1994-69290	19940519
AU 689779	B2	19980409		
EP 703981	A1	19960403	EP 1994-917653	19940519
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

JP 08510120	T2	19961029	JP 1994-524997	19940519
US 6248330	B1	20010619	US 1995-432697	19950502
US 5843460	A	19981201	US 1995-467822	19950606
US 6258359	B1	20010710	US 1995-466248	19950606
AU 9875081	A1	19981001	AU 1998-75081	19980709
AU 724584	B2	20000928		

PRIORITY APPLN. INFO.:

EP 1993-401309	A	19930519
WO 1993-EP3259	A	19931119
WO 1994-EP1625	W	19940519
US 1995-432697	A2	19950502
US 1995-447177	A1	19950519

AB The invention relates to an immunogenic compn., capable of inducing protective antibodies against Helicobacter infection, characterized in that it comprises: i) at least one subunit of a urease structural polypeptide from Helicobacter pylori, or a fragment thereof, said fragment being recognized by antibodies reacting with Helicobacter felis urease, and/or at least one subunit of a urease structural polypeptide from Helicobacter felis, or a fragment thereof, said fragment being recognized by antibodies reacting with Helicobacter pylori urease; ii) optionally, a urease-assocd. Heat Shock protein (HSP), or chaperonin, from Helicobacter, or a fragment of said protein.

IT **151187-40-5P**, Urease (Helicobacter felis strain ATCC 49179 gene ureB .beta.-6 subunit reduced) **162243-38-1P 162243-40-5P**, Urease (Helicobacter felis gene ureA) **162243-42-7P**, Urease (Helicobacter felis gene ureI) **167293-79-0P**
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence of; immunogenic compns. against Helicobacter infection, polypeptides for use in compns. and nucleic acid sequences encoding said polypeptides)

IT **162243-39-2 162243-43-8**, Deoxyribonucleic acid (Helicobacter felis gene ureI) **167293-74-5 167293-75-6 167293-76-7 167293-77-8 167293-78-9**
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(nucleotide sequence of; immunogenic compns. against Helicobacter infection, polypeptides for use in compns. and nucleic acid sequences encoding said polypeptides)

IT **9002-13-5P**, Urease
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(subunit A and subunit B; immunogenic compns. against Helicobacter infection, polypeptides for use in compns. and nucleic acid sequences encoding said polypeptides)

L7 ANSWER 54 OF 63 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER:	1995:702389 HCAPLUS
DOCUMENT NUMBER:	123:167008
TITLE:	Oral immunization with recombinant Helicobacter pylori urease induces secretory IgA antibodies and protects mice from challenge with Helicobacter felis
AUTHOR(S):	Lee, Cynthia K.; Weltzin, Richard; Thomas, William D.; Kleanthous, Harold; Ermak, Thomas H.; Soman, Gopalan; Hill, Joseph E.; Ackerman, Samuel K.; Monath, Thomas P.
CORPORATE SOURCE:	OraVax Inc., Cambridge, MA, 02139, USA
SOURCE:	J. Infect. Dis. (1995), 172(1), 161-72 CODEN: JIDIAQ; ISSN: 0022-1899
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB Helicobacter pylori, a gram-neg. spiral bacterium, is the cause of chronic superficial (type B) **gastritis** and peptic **ulcer** disease. The urease enzyme of H. pylori was expressed as an inactive recombinant protein in Escherichia coli, purified as particulate structures of 550-600 kDa mol. mass with a diam. of .apprx. 12 nm. Given orally, 5 .mu.g of urease with an appropriate mucosal adjuvant, such as the labile toxin of E. coli, protected 60%-100% of mice against challenge with virulent Helicobacter felis. Protection correlated with the level of secretory IgA antibodies against urease. Oral administration of antigen was as effective or better than **intragastric** administration. Parenteral injection of antigen or **intragastric** administration of high-dose antigen without adjuvant elicited serum IgG but no IgA antibodies and did not confer protection. Recombinant urease as an oral **vaccine** candidate deserves further investigation as an approach to the prevention of Helicobacter-induced chronic **gastroduodenal** diseases in humans.

IT **9002-13-5**, Urease
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(oral immunization with recombinant Helicobacter pylori urease induces secretory IgA and protects mice from challenge with H. felis)

L7 ANSWER 55 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:676998 HCAPLUS
DOCUMENT NUMBER: 123:81196
TITLE: The GroES homolog of Helicobacter pylori confers protective immunity against mucosal infection in mice
AUTHOR(S): Ferrero, Richard L.; Thiberge, Jean-Michel; Kansau, Imad; Wuscher, Nicole; Huerre, Michel; Labigne, Agnes
CORPORATE SOURCE: Unite Enterobacteries, Inst. Natl. Sante Rech. Med. U389, Paris, 75724, Fr.
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1995), 92(14), 6499-503
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Helicobacter pylori is an important etiol. agent of **gastroduodenal** disease. In common with other organisms, H. pylori bacteria express heat shock proteins that share homologies with the GroES-GroEL class of proteins from Escherichia coli. The authors have assessed the heat shock proteins of H. pylori as potential protective antigens in a murine model of **gastric** Helicobacter infection. **Orogastric** immunization of mice with recombinant H. pylori GroES- and GroEL-like proteins protected 80% and 70% of animals, resp., from a challenge dose of 104 Helicobacter felis bacteria (compared to control mice, and, resp.). All mice that were immunized with a dual antigen prepn., consisting of H. pylori GroES-like protein and the B subunit of H. pylori urease, were protected against infection. This represented a level of protection equiv. to that provided by a sonicated Helicobacter ext. Antibodies directed against the recombinant H. pylori antigens were predominantly of the IgG1 class, suggesting that a type 2 T-helper cell response was involved in protection. This work reports a protein belonging to the GroES class of heat shock proteins that was shown to induce protective immunity. In conclusion, GroES-like and urease B-subunit proteins have been identified as potential components of a future H. pylori subunit **vaccine**.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protective immunity against Helicobacter pylori mucosal infection is induced by HspA protein and B subunit of)

L7 ANSWER 56 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:634741 HCAPLUS
DOCUMENT NUMBER: 123:17850
TITLE: Oral **vaccines** containing urease antigen for prevention or treatment of Helicobacter infections
INVENTOR(S): Leveen, Harry H.; Laveen, Eric G.; Laveen, Robert F.
PATENT ASSIGNEE(S): USA
SOURCE: Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 654273	A1	19950524	EP 1994-308551	19941118
R: DE, FR, GB, IT				

PRIORITY APPLN. INFO.: US 1993-153856 19931118
US 1993-153857 19931118
US 1994-185749 19940124

AB Oral **vaccines** contg. a non-enzymic urease antigen for treating and/or preventing Helicobacter infections. Acid urease was obtained from culture of lactobacillus fermentum and was reacted with glutaraldehyde to form a non-enzymic urease antigen. Mice were immunized with the inactive urease antigen prior to the challenging dose of Helicobacter felis were protected from development of **gastritis**. The infecting organism could not be recovered from the **gastric** content and was not present on histol. examn. of **gastric** tissue.

IT **9002-13-5**, Urease
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antigen; oral **vaccines** contg. urease antigen for prevention or treatment of Helicobacter infections)

L7 ANSWER 57 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:467429 HCAPLUS
DOCUMENT NUMBER: 122:237257
TITLE: Effect of oral immunization with recombinant urease on murine Helicobacter felis **gastritis**
AUTHOR(S): Pappo, J.; Thomas, W. D., Jr.; Kabok, Z.; Taylor, N. S.; Murphy, J. C.; Fox, J. G.
CORPORATE SOURCE: Vaccine Delivery Res. Microbiol. Sections, Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SOURCE: Infect. Immun. (1995), 63(4), 1246-52
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The ability of oral immunization to interfere with the establishment of infection with Helicobacter felis was examd. Groups of Swiss Webster mice were immunized orally with 250 .mu.g of Helicobacter pylori recombinant urease (rUrease) and 10 .mu.g of cholera toxin (CT) adjuvant, 1 mg of H. felis sonicate antigens and CT, or phosphate-buffered saline (PBS) and CT. Oral immunization with rUrease resulted in markedly elevated serum IgG (IgG), serum IgA, and intestinal IgA antibody responses. Challenge with live H. felis further stimulated the urease-specific intestinal IgA and serum IgG and IgA antibody levels in mice previously immunized with rUrease but activated primarily the serum IgG compartment of PBS-treated and H. felis-immunized mice. Intestinal IgA and serum IgG and IgA

anti-urease antibody responses were highest in rUrease-immunized mice at the termination of the expt. Mice immunized with rUrease were significantly protected against infection when challenged with H. felis 2 or 6 wk post-oral immunization in comparison with PBS-treated mice. Whereas H. felis-infected mice displayed multifocal **gastric** mucosal lymphoid follicles consisting of CD45R+ B cells surrounded by clusters of Thy1.2+ T cells, **gastric** tissue from rUrease-immunized mice contained few CD45R+ B cells and infrequent mucosal follicles. These observations show that oral immunization with rUrease confers protection against H. felis infection and suggest that **gastric** tissue may function as an effector organ of the mucosal immune system which reflects the extent of local antigenic stimulation.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of oral immunization with recombinant urease on murine Helicobacter felis **gastritis** and Ig levels)

L7 ANSWER 58 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:442082 HCAPLUS
DOCUMENT NUMBER: 122:236681
TITLE: Development of a mouse model of Helicobacter pylori infection that mimics human disease
AUTHOR(S): Marchetti, Marta; Arico, Beatrice; Burroni, Daniela; Figura, Natale; Rappuoli, Rino; Ghiara, Paolo
CORPORATE SOURCE: IRIS, Biocine SpA, Siena, 53100, Italy
SOURCE: Science (Washington, D. C.) (1995), 267(5204), 1655-8
CODEN: SCIEAS; ISSN: 0036-8075
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The human pathogen Helicobacter pylori is assocd. with **gastritis**, peptic **ulcer** disease, and **gastric** cancer. The pathogenesis of H. pylori infection in vivo was studied by adapting fresh clin. isolates of bacteria to colonize the stomachs of mice. A **gastric** pathol. resembling human disease was obsd. in infections with cytotoxin-producing strains but not with noncytotoxic strains. Oral immunization with purified H. pylori antigens protected mice from bacterial infection. This mouse model will allow the development of therapeutic agents and **vaccines** against H. pylori infection in humans.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protection from Helicobacter pylori infection of mouse by immunization using)

L7 ANSWER 59 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:698698 HCAPLUS
DOCUMENT NUMBER: 121:298698
TITLE: Recombinant antigens prepared from the urease subunits of Helicobacter spp.: evidence of protection in a mouse model of **gastric** infection
AUTHOR(S): Ferrero, Richard L.; Thiberge, Jean-Michel; Huerre, Michel; Labigne, Agnes
CORPORATE SOURCE: Unite Enterobacteries, Inst. Pasteur, Paris, 75724, Fr.
SOURCE: Infect. Immun. (1994), 62(11), 4981-9
CODEN: INFIBR; ISSN: 0019-9567
DOCUMENT TYPE: Journal
LANGUAGE: English

Minnifield 09/955,739

AB Urease is an important virulence factor for **gastric** Helicobacter spp. To elucidate the efficacy of individual urease subunits to act as mucosal immunogens, the genes encoding the resp. urease subunits (UreA and UreB) of Helicobacter pylori and Helicobacter felis were cloned in an expression vector (pMAL) and expressed in Escherichia coli cells as translational fusion proteins. The recombinant UreA and UreB proteins were purified by affinity and anion-exchange chromatog. techniques and had predicted mol. masses of approx. 68 to 103 kDa, resp. Western blotting (immunoblotting) studies indicated that the urease components of the fusion proteins were strongly immunogenic and were specifically recognized by polyclonal rabbit anti-Helicobacter sp. sera. The fusion proteins (50 .mu.g) were used, in combination with a mucosal adjuvant (cholera toxin), to **orogastrically** immunize mice against H. felis infection. **Gastric** tissues from H. felis-challenged mice were assessed by the biopsy urease test and by histol. In mice immunized with recombinant H. felis UreB, 60% of animals (n = 7) were histol. neg. for H. felis bacteria after challenge at 17 wk. This compared with 25% (n = 8) for mice immunized with the heterologous H. pylori UreB antigen. Neither the homologous nor the heterologous UreA subunit elicited protective responses against H. felis infection in mice. The study demonstrated that a recombinant subunit antigen could induce an immunoprotective response against **gastric** Helicobacter infection.

IT **9002-13-5**, Urease
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(recombinant urease subunits induce protective immunity against Helicobacter species)

L7 ANSWER 60 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:291205 HCAPLUS
DOCUMENT NUMBER: 120:291205
TITLE: Gene Structure of the Helicobacter pylori Cytotoxin and Evidence of Its Key Role in **Gastric** Disease
AUTHOR(S): Telford, John L.; Ghiara, Paolo; Dell'Orco, Mariangela; Comanducci, Maurizio; Burroni, Daniela; Bugnoli, Massimo; Tecce, Mario F.; Censini, Stefano; Covacci, Antonello; et al.
CORPORATE SOURCE: Dep. Mol. Biol., Res. Inst. Siena, Siena, 53100, Italy
SOURCE: J. Exp. Med. (1994), 179(5), 1653-8
CODEN: JEMEAV; ISSN: 0022-1007
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The gram neg., microaerophilic bacterium Helicobacter pylori colonizes the human **gastric** mucosa and establishes a chronic infection that is tightly assocd. with atrophic **gastritis**, peptic **ulcer**, and **gastric** carcinoma. Cloning of the H. pylori cytotoxin gene shows that the protein is synthesized as a 140-kD precursor that is processed to a 94-kD fully active toxin. Oral administration to mice of the purified 94-kD protein caused **ulceration** and **gastric** lesions that bear some similarities to the pathol. obsd. in humans. The cloning of the cytotoxin gene and the development of a mouse model of human **gastric** disease will provide the basis for the understanding of H. pylori pathogenesis and the development of therapeutics and **vaccines**.

IT **154984-93-7**, Cytotoxin (Helicobacter pylori precursor)
RL: PRP (Properties)
(amino acid sequence of and **ulceration** and **gastric** lesions induced in mice by)

IT **154984-92-6**, DNA (Helicobacter pylori cytotoxin gene plus flanks)

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RL: PRP (Properties); BIOL (Biological study)
(nucleotide sequence of)

L7 ANSWER 61 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:2256 HCAPLUS
DOCUMENT NUMBER: 120:2256
TITLE: Helicobacter pylori proteins useful for **vaccines** and diagnostics
INVENTOR(S): Covacci, Antonello; Bugnoli, Massimo; Telford, John; Macchia, Giovanni; Rappuoli, Rino
PATENT ASSIGNEE(S): Biocine Sclavo S.p.A., Italy
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9318150	A1	19930916	WO 1993-EP472	19930302
W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9336300	A1	19931005	AU 1993-36300	19930302
EP 643770	A1	19950322	EP 1993-905285	19930302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07504565	T2	19950525	JP 1993-515309	19930302
EP 967279	A1	19991229	EP 1999-202698	19930302
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
JP 2000333686	A2	20001205	JP 2000-126696	19930302
JP 2000350591	A2	20001219	JP 2000-126695	19930302
US 6077706	A	20000620	US 1995-470260	19950606
US 6130059	A	20001010	US 1995-466662	19950606

PRIORITY APPLN. INFO.:

IT 1992-FI52	A	19920302
WO 1993-EP158	A	19930125
EP 1993-905285	A3	19930302
JP 1993-515309	A	19930302
WO 1993-EP472	A	19930302
US 1994-256848	B3	19941021

AB The H. pylori genes for cytotoxin, CAI (cytotoxin-assocd. immunodominant) antigen, and heat-shock protein (of the hsp60 family) are cloned and sequenced. The nucleic acids and proteins may be used for diagnosis and the proteins for **vaccination** against H. pylori. The cytotoxin, or CT antigen, gene encoded a 140 kDa protein precursor of a 100 kDa protein with urease-independent vaculolating activity. The CAI antigen gene was absent in noncytotoxic H. pylori strains. The heterogeneity of the CAI antigen appeared to be due to internal duplications in the gene: strain G39 was found to have two identical repeats of a 102 bp sequence within the gene. The heat-shock protein gene was expressed in all H. pylori strains tested, both cytotoxic and noncytotoxic. Most sera from patients infected with H. pylori and exhibiting **gastritis** and **ulcers** contained antibodies to the hsp, but the degree of recognition varied greatly among the patients and the antibody levels did not show any obvious correlation with the type of disease.

IT **151354-79-9**, CAI antigen (Helicobacter pylori strain CCUG 17874 clone A1) **151441-76-8**, Heat-shock protein (Helicobacter pylori clone pHp60G5) **151639-33-7**, Cytotoxin (Helicobacter pylori clone

TOXEE1 precursor) **151639-36-0**, CAI antigen (Helicobacter pylori strain G39)
RL: PRP (Properties)
(amino acid sequence of)

IT **149738-23-8**, DNA (Helicobacter pylori strain CCUG 17874 clone A1 CAI antigen gene and flanks) **151243-14-0**, DNA (Helicobacter pylori clone pHp60G5 heat-shock protein gene and flanks) **151639-32-6**, DNA (Helicobacter pylori clone TOXEE1 cytotoxin gene and flanks) **151639-35-9**, DNA (Helicobacter pylori strain G39 CAI antigen gene and flanks)
RL: PRP (Properties); BIOL (Biological study)
(nucleotide sequence of)

L7 ANSWER 62 OF 63 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:664549 HCAPLUS
DOCUMENT NUMBER: 119:264549
TITLE: Purified vacuolating toxin from Helicobacter pylori and its use in diagnosis and **vaccines**
INVENTOR(S): Cover, Timothy L.; Blaser, Martin J.
PATENT ASSIGNEE(S): Vanderbilt University, USA
SOURCE: PCT Int. Appl., 75 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9316723	A1	19930902	WO 1993-US1558	19930224
W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG				
AU 9337282	A1	19930913	AU 1993-37282	19930224
EP 629132	A1	19941221	EP 1993-906142	19930224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 07507444	T2	19950824	JP 1993-515007	19930224
US 6054132	A	20000425	US 1994-284747	19940802
US 5859219	A	19990112	US 1994-295643	19941027
US 6013463	A	20000111	US 1995-473265	19950607

PRIORITY APPLN. INFO.: US 1992-841644 19920226
WO 1993-US1558 19930224
US 1994-284747 19940802

AB H. pylori, a causative agent of chronic **gastritis**, produces a toxin (CB antigen) which can be used as a basis for **vaccines** and for producing antibodies for diagnostic tests. The toxin, purified chromatog. from H. pylori, had an N-terminal amino acid sequence partially homologous to those of various ion channel proteins and permeases. Portions of the toxin gene were amplified by PCR, cloned, and sequenced. A neutralizing antiserum to the toxin was produced in rabbits and used for detection of the toxin. An ELISA is described for detection of anti-toxin antibodies in human serum for diagnosis of infection with toxigenic H. pylori. Cellular damage (vacuolation) from the toxin was prevented in HeLa cells by bafilomycin A1, an inhibitor of vacuolar-type ATPase.

IT **151441-14-4**
RL: PRP (Properties); BIOL (Biological study)
(nucleotide sequence and cloning of)

L7 ANSWER 63 OF 63 HCAPLUS COPYRIGHT 2002 ACS

Minnifield 09/955,739

ACCESSION NUMBER: 1991:651669 HCAPLUS
DOCUMENT NUMBER: 115:251669
TITLE: A method for the stepwise, controlled synthesis of chemical species, particularly peptides, on protein substrates, coupled products obtained by the method, and the use of these coupled products, e.g. as **vaccines**
INVENTOR(S): Houen, Gunnar; Holm, Arne
PATENT ASSIGNEE(S): Den.
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9108220	A1	19910613	WO 1990-DK311	19901130
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, GR, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, RO, SD, SE, SU, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
AU 9168929	A1	19910626	AU 1991-68929	19901130
PRIORITY APPLN. INFO.:			DK 1989-6085	19891201
			WO 1990-DK311	19901130

AB Chem. species, esp. peptides, are synthesizied by a stepwise, controlled process using a proteinaceous substances as the synthesis substrate. The coupled products obtained by the process can be used, e.g., as **vaccines**, matrix materials, or carrier mols. The products, including peptides and peptide derivs., prepd. by the method are also claimed. Bovine serum albumin (BSA) was placed in a silylated reaction vessel and the CO2H groups were diethylamidated before coupling glutamic acid as the Fmoc (9-fluorenylmethyloxycarbonyl) and tert-Bu protected Dhbt (3-hydroxy-3,4-dihydrobenzotriazin-4-one ester, blocking remaining amino groups with acetic anhydride, and sequentially coupling Fmoc- and side chain-protected Dhbt esters of lysine, serine, threonine, aspartic acid, methionine, and serine. Piperidine was used to remove the Fmoc protecting group between couplings. Side chain protection groups were removed in CH2Cl2/F3CCO2H (1:1 vol./vol.) at 0.degree.. The product had an av. of 35 synthesized peptide chains per BSA mol. The coupled product was used to raise antibodies to Ser-Met-Asp-Thr-Ser-Lys-Glu in rabbits.

IT **9002-13-5**, Urease
RL: ANST (Analytical study)
(as carrier for peptide synthesis)

Searched by Mona Smith

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File   5:Biosis Previews(R) 1969-2002/Jul W2
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         (c) 2002 Inst for Sci Info
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         (c) 2002 ProQuest Info&Learning
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         (c) 2002 Cambridge Sci Abs
File 144:Pascal 1973-2002/Jul W3
         (c) 2002 INIST/CNRS
File 162:CAB HEALTH 1983-2002/Jun
         (c) 2002 CAB INTERNATIONAL
File 345:Inpadoc/Fam.& Legal Stat 1968-2002/UD=199970
         (c) 2002 EPO
File 351:Derwent WPI 1963-2002/UD,UM &UP=200246
         (c) 2002  Thomson Derwent
File 357:Derwent Biotech Res. 1982-2002/June W1
         (c) 2002 Thomson Derwent & ISI
File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
File 440:Current Contents Search(R) 1990-2002/Jul 23
         (c) 2002 Inst for Sci Info
?ds

Set     Items   Description
S1        731   (H OR HELICOBACTER?)(S)UREASE? AND VACCIN?
S2        258   RD (unique items)
S3        248   S2 AND (GASTR? OR ULCER? OR INTEST? OR STOMACH? OR METAPLA-
            SIA? OR LYMPHOMA? OR PYLORI OR FELIS)
S4        142   S2(S)(GASTRI? OR GASTRO? OR ULCER? OR INTESTIN? OR STOMACH?
             OR METAPLASIA? OR LYMPHOMA?)
S5         80   S4 AND PY=(2002 OR 2001 OR 1999 OR 1998 OR 1997)
S6         62   S4 NOT S5
?t6/3 ab/1-62
>>>No matching display code(s) found in file(s): 65, 345

 6/AB/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10872412   20432624   PMID: 10974142
  Quantitative and bioluminescent assay to measure efficacy of conventional
and DNA vaccinations against Helicobacter pylori.
  Ozpolat B; Rao X M; Lachman L B; Osato M S; Graham D Y
  Department of Bioimmunotherapy, University of Texas M. D. Anderson Cancer
Center, Houston, TX 77030, USA.
  Combinatorial chemistry & high throughput screening (NETHERLANDS)   Aug
2000, 3 (4) p289-302, ISSN 1386-2073   Journal Code: 9810948
  Contract/Grant No.: CA16672; CA; NCI
  Document type: Journal Article
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Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Vaccination against Helicobacter pylori using DNA sequences encoding Urease A and B subunits was compared to immunization with urease antigen and MTP-PE in a liposome formulation. To determine the effectiveness of a vaccine against H . pylori in a mouse model it is essential to quantify the number of H . pylori remaining in the stomachs following challenge with an inoculum of live bacteria. Culture assays and enzymatic assays produce inconsistent results often unsuitable to conclude if vaccine candidates are protective. To overcome this problem, we developed two assays: 1) a competitive quantitative PCR using a colorimetric readout and 2) a non-competitive direct quantitative PCR using a highly sensitive bioluminescent readout. The competitive PCR requires coamplification of a segment of the urease C sequence and an internal control standard in a competitive manner using a single set of primers. PCR products were quantified colorimetrically by an enzyme-linked immunosorbent assay and compared with known quantities of the internal control standard added to the PCR reaction. The highly sensitive, bioluminescent assay measures the amplified DNA directly using a flash-type luminescent tag and a specific probe. The Sydney strain of H . pylori was used for the mouse infection model. Quantification of H . pylori by either the bioluminescent assay or the competitive PCR was reliable, specific and sensitive compared to quantitative growth assays which often gave false results. The bioluminescent assay was much more sensitive and less labor/time intensive than the competitive PCR. The bioluminescent assay was able to quantitate as few as 100 bacteria, while the competitive assay could not detect less than 10(3) bacteria per mouse stomach . Quantification of H . pylori by bioluminescent assay was superior to the competitive assay and may be used for research applications, such as the development of vaccines , pathogenesis of gastric disease and monitoring of antibiotic treatment.

6/AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10851595 20380106 PMID: 10926118

The mucosal adjuvanticity of two nontoxic mutants of Escherichia coli heat-labile enterotoxin varies with immunization routes.

Park E J; Chang J H; Kim J S; Yum J S; Chung S I
Mogam Biotechnology Research Institute, Yonginsi, Kyonggido, Korea.

Experimental & molecular medicine (KOREA (SOUTH)) Jun 30 2000, 32 (2) p72-8, ISSN 1226-3613 Journal Code: 9607880
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Escherichia coli heat-labile enterotoxin (LT), which causes a characteristic diarrhea in humans and animals, is a strong mucosal immunogen and has powerful mucosal adjuvant activity towards coadministered unrelated antigens. Here we report the different mucosal adjuvanticity of nontoxic LT derivatives, LTS63Y and LTdelta110/112, generated by immunizing through two different mucosal routes. Intragastric (IG) immunization with Helicobacter pylori urease alone resulted in poor systemic IgG and IgA responses and no detectable local secretory IgA, but IG co-immunization with urease and LTdelta110/112 induced high titers of urease -specific local secretory IgA and systemic IgG and IgA, comparable to those induced by wild-type LT. LTS63Y showed far lower adjuvant activity towards urease than LTdelta110/112 in IG immunization, but was more active than LTdelta110/112 in inducing immune responses to urease by intranasal (IN) immunization. LTdelta110/112 predominantly enhanced the induction of

urease -specific IgG1 levels following IG immunization, whereas LTS63Y induced high levels of IgG1, IgG2a and IgG2b following IN immunization. In addition, quantitative H . pylori culture of stomach tissue following challenge with H . pylori demonstrated a 90-95% reduction ($p < 0.0002$) in bacterial burden in mice immunized intranasally with urease using either mutant LT as an adjuvant. These results indicate that the mechanism(s) underlying the adjuvant activities of mutant LTs towards coadmnistered H . pylori urease may differ between the IN and IG mucosal immunization routes.

6/AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10760102 20291464 PMID: 10828751
Challenges to therapy in the future.
O'Morain C; Montague S
Gastroenterology Department, Adelaide and Meath Hospital, Tallaght, Dublin, Ireland.
Helicobacter (UNITED STATES) 2000, 5 Suppl 1 pS23-6; discussion S27-31, ISSN 1083-4389 Journal Code: 9605411
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Quadruple therapy (with a proton pump inhibitor (PPI), metronidazole, tetracycline and bismuth) is generally reserved for second-line treatment; however, studies using this regimen for 7 days have found it to be effective even in metronidazole-resistant strains. Resistance is an ongoing problem with antimicrobial therapy but considerable progress has now been made into understanding the underlying genetic mechanisms of this process. Metronidazole resistance in Europe is usually in the range of 20-30% of strains but may be as high as 70% in some countries. One genetic mechanism involved is thought to be a mutation of the rdxA gene. Macrolide resistance appears to be on the increase in Europe, varying from 1% in some countries to 13% in others. The genetic mechanism involved has been shown to be a point mutation of a ribosomal RNA. Amoxicillin resistance is an emerging problem that has an adverse effect on eradication rates in clinical practice. Resistance has been shown to be caused by the absence of one of the four binding proteins in the cell wall. Few novel antibiotics have been developed for use in eradication therapy, although rifabutin, secnidazole and furazolidone have shown some success as part of combination therapy. Alternative therapies that have been tested include mucosal protective agents which have been used in place of a PPI in some eradication regimens with some success, and the somatostatin analog, octreotide, that has been used as part of quadruple therapy in place of a PPI and produced eradication rates of approximately 88%. The ultimate challenge is still to develop a safe and effective vaccine against Helicobacter pylori. Current and future research will also focus on identifying genetic targets for therapy, adhesion molecule analogs to prevent binding of the bacterium, and urease inhibitors. The current triple therapy treatment options available for the eradication of Helicobacter pylori infection are over 90% effective in susceptible organisms and there are very few medical conditions to which we can offer such efficacious treatment. Unfortunately, the recommendations made at consensus conferences are not always put into practice and physicians in primary care may be unaware of the true efficacy of eradication therapy. Treatment is very simple: three drugs, twice a day for 1 week. The main focus for both primary care physicians and gastroenterologists should be to reinforce the need for patient compliance, otherwise we will see an increase in antibiotic resistance. Patients should be prewarned that they may experience some mild side

effects and should be encouraged to complete the course of treatment. The real challenge for the future will be the management of patients who do not respond to first-line treatment. This paper will focus on potential problems with therapy, such as antibiotic resistance, and possible future solutions, such as novel antibiotics and vaccines .

6/AB/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10707114 20245734 PMID: 10781854
Further development of the Helicobacter pylori mouse vaccination model.
Sutton P; Wilson J; Lee A
School of Microbiology and Immunology, University of New South Wales, Sydney, Australia.
Vaccine (ENGLAND) Jun 1 2000, 18 (24) p2677-85, ISSN 0264-410X
Journal Code: 8406899
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Immunisation against Helicobacter infection in mouse models has thus far produced neither complete protection against the bacteria, nor a complete prevention of the associated gastritis . This study aimed firstly to compare the sensitivities of the various methods used to assess H . pylori infection in the mouse model, and secondly to develop the experimental design to induce a more effective immunity, aimed at further reducing bacterial burden in the gastric tissue. Various mouse strains were prophylactically immunised with whole bacterial sonicate and cholera toxin before challenge with H . pylori-SS1. The relative sensitivities of the urease assay, histological assessment and the colony forming assay to detect levels of H . pylori colonisation were compared. Comparisons of different antigen doses and different timecourses of immunisation were performed. The colony forming assay was found to be far more sensitive than either the urease assay or histological assessment for determining the protective efficacies of immunisation. Mice which had 10(5) H . pylori per gram of stomach by colony assay were negative by histology and urease . Lower doses of whole cell sonicate were more protective than high doses and more effective immunisation was achieved by leaving at least 3 weeks between immunisation instead of weekly immunisations. In conclusion, for assessment of H . pylori colonisation in the mouse model, the colony forming assay should be used. The experimental protocol for immunisation has been altered to produce a significant improvement in protection. However, full protection has still not yet been achieved and more work is still required.

6/AB/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10700293 20231817 PMID: 10768972
Parenteral adjuvant activities of Escherichia coli heat-labile toxin and its B subunit for immunization of mice against gastric Helicobacter pylori infection.
Weltzin R; Guy B; Thomas W D; Giannasca P J; Monath T P
OraVax, Inc., Cambridge, Massachusetts 02139, USA. rweltzin@oravax.com
Infection and immunity (UNITED STATES) May 2000, 68 (5) p2775-82, ISSN 0019-9567 Journal Code: 0246127
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM

Record type: Completed
The heat-labile toxin (LT) of Escherichia coli is a potent mucosal adjuvant that has been used to induce protective immunity against Helicobacter felis and Helicobacter pylori infection in mice. We studied whether recombinant LT or its B subunit (LTB) has adjuvant activity in mice when delivered with H . pylori urease antigen via the parenteral route. Mice were immunized subcutaneously or intradermally with urease plus LT, recombinant LTB, or a combination of LT and LTB prior to intragastric challenge with H . pylori. Control mice were immunized orally with urease plus LT, a regimen shown previously to protect against H . pylori gastric infection. Parenteral immunization using either LT or LTB as adjuvant protected mice against H . pylori challenge as effectively as oral immunization and enhanced urease -specific immunoglobulin G (IgG) responses in serum as effectively as aluminum hydroxide adjuvant. LT and LTB had adjuvant activity at subtoxic doses and induced more consistent antibody responses than those observed with oral immunization. A mixture of a low dose of LT and a high dose of LTB stimulated the highest levels of protection and specific IgG in serum. Urease -specific IgG1 and IgG2a antibody subclass responses were stimulated by all immunization regimens tested, but relative levels were dependent on the adjuvant used. Compared to parenteral immunization with urease alone, LT preferentially enhanced IgG1, while LTB or the LT-LTB mixture preferentially enhanced IgG2a. Parenteral immunization using LT or LTB as adjuvant also induced IgA to urease in the saliva of some mice. These results show that LT and LTB stimulate qualitatively different humoral immune responses to urease but are both effective parenteral adjuvants for immunization of mice against H . pylori infection.

6/AB/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10700265 20231789 PMID: 10768944
Immunization with recombinant Helicobacter pylori urease in specific-pathogen-free rhesus monkeys (Macaca mulatta).
Solnick J V; Canfield D R; Hansen L M; Torabian S Z
Department of Internal Medicine (Division of Infectious Diseases), University of California, Davis School of Medicine, Davis, California 95616, USA. jvsolnick@ucdavis.edu
Infection and immunity (UNITED STATES) May 2000, 68 (5) p2560-5, ISSN 0019-9567 Journal Code: 0246127
Contract/Grant No.: AI-42081; AI; NIAID; RR00169; RR; NCRR
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Immunization with urease can protect mice from challenge with Helicobacter pylori, though results vary depending on the particular vaccine , challenge strain, and method of evaluation. Unlike mice, rhesus monkeys are naturally colonized with H . pylori and so may provide a better estimate of vaccine efficacy in humans. The purpose of this study was to examine the effectiveness of H . pylori urease as a vaccine in specific-pathogen (H . pylori)-free rhesus monkeys. Monkeys raised from birth and documented to be free of H . pylori were vaccinated with orogastric (n = 4) or intramuscular (n = 5) urease . Two control monkeys were sham vaccinated . All monkeys were challenged with a rhesus monkey-derived strain of H . pylori, and the effects of vaccination were evaluated by use of quantitative cultures of gastric tissue, histology, and measurement of serum immunoglobulin G (IgG) and salivary IgA. Despite a humoral immune response, all monkeys were infected after H . pylori challenge, and there were no differences in the density of colonization.

Immunization with urease therefore does not fully protect against challenge with H . pylori. An effective vaccine to prevent H . pylori infection will require different or more likely additional antigens, as well as improvements in the stimulation of the host immune response.

6/AB/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10641518 20187487 PMID: 10722611
Pilot study of phoP/phoQ-deleted Salmonella enterica serovar typhimurium expressing Helicobacter pylori urease in adult volunteers.
Angelakopoulos H; Hohmann E L
Infectious Disease Division, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts 02114, USA.
Infection and immunity (UNITED STATES) Apr 2000, 68 (4) p2135-41, ISSN 0019-9567 Journal Code: 0246127
Contract/Grant No.: MO1 RR01066-21; RR; NCRR; RO1AI45137; AI; NIAID
Document type: Clinical Trial; Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Attenuated Salmonella enterica serovar Typhi has been studied as an oral vaccine vector. Despite success with attenuated S. enterica serovar Typhimurium vectors in animals, early clinical trials of S. enterica serovar Typhi expressing heterologous antigens have shown that few subjects have detectable immune responses to vectored antigens. A previous clinical study of phoP/phoQ-deleted S. enterica serovar Typhi expressing Helicobacter pylori urease from a multicopy plasmid showed that none of eight subjects had detectable immune responses to the vectored antigen. In an attempt to further define the variables important for engendering immune responses to vectored antigens in humans, six volunteers were inoculated with 5 x 10(7) to 8 x 10(7) CFU of phoP/phoQ-deleted S. enterica serovar Typhimurium expressing the same antigen. Two of the six volunteers had fever; none had diarrhea, bacteremia, or other serious side effects. The volunteers were more durably colonized than in previous studies of phoP/phoQ-deleted S. enterica serovar Typhi. Five of the six volunteers seroconverted to S. enterica serovar Typhimurium antigens and had strong evidence of anti-Salmonella mucosal immune responses by enzyme-linked immunospot studies. Three of six (three of five who seroconverted to Salmonella) had immune responses in the most sensitive assay of urease -specific immunoglobulin production by blood mononuclear cells in vitro. One of these had a fourfold or greater increase in end-point immunoglobulin titer in serum versus urease . Attenuated S. enterica serovar Typhimurium appears to be more effective than S. enterica serovar Typhi for engendering immune responses to urease . Data suggest that this may be related to a greater stability of antigen-expressing plasmid in S. enterica serovar Typhimurium and/or prolonged intestinal colonization. Specific factors unique to nontyphoidal salmonellae may also be important for stimulation of the gastrointestinal immune system.

6/AB/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10611753 20154333 PMID: 10689743
Accuracy of 13C-urea breath test in clinical use for diagnosis of Helicobacter pylori infection.
Riepl R L; Folwaczny C; Otto B; Klauser A; Blendinger C; Wiebecke B; Konig A; Lehnert P; Heldwein W
Medizinische Klinik, Klinikum Innenstadt, Ludwig-Maximilians-Universitat

Munchen, Germany.
Zeitschrift fur Gastroenterologie (GERMANY) Jan 2000, 38 (1) p13-9,
ISSN 0044-2771 Journal Code: 0033370
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The 13C-urea breath test (UBT) is a noninvasive test for diagnosis of Helicobacter pylori infection of gastric mucosa. The aim of this prospective study was to assess the accuracy of a simple UBT in clinical routine use. METHODS: The study population comprised of 100 patients (49 f, 51 m) requiring diagnostic upper GI endoscopy. One biopsy specimen was taken from the gastric antrum, body and fundus, respectively, for standard histological examination and one additional specimen from each location was transformed into transport medium for cultivation of H . pylori. After vaccination of the culture plates the biopsies were tested for urease activity (UAT). After recovery from endoscopy the patients had to pass an one liter endexspiratory breath sample before and 15 min after drinking 200 ml orange juice, pH 3.6, containing 75 mg of 13C-urea. 13CO2 was measured in the breath samples using isotope-selective nondispersive infrared spectrometry. RESULTS: Defining gold standard groups with all biopsy tests (from antrum and corpus) positive or negative the 13CO2 delta over baseline (DOB) cut-off level of UBT was set at 6.5/1000 in order to best discriminate positive from negative patients (ROC analysis). UBT was positive in 37% of all subjects. Taken UAT and histological examination together (positive when both tests were positive) UBT displayed a sensitivity of 92%, a specificity of 94%, a positive predictive value of 89%, and a negative predictive value of 94%. When including the results of culture sensitivity and negative predictive value reached almost 100%. The mean of the 13CO2-DOB values from H . pylori-positive duodenal or gastric ulcer patients did not differ from controls (H . pylori-positive patients without lesions). The 13CO2-DOB values of the ulcer group were correlated significantly with the active inflammatory component of gastritis in antrum, corpus, and fundus. CONCLUSION: UBT with this setup detects H . pylori infection in clinical routine use with high accuracy. The increase of exhaled 13CO2 does not predict ulcer disease but reflects the degree of active inflammation of gastric mucosa.

6/AB/9 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09243461 97118683 PMID: 8959525
Vaccination against Helicobacter pylori.
Lee A
School of Microbiology and Immunology, University of New South Wales, Sydney, Australia.
Journal of gastroenterology (JAPAN) Nov 1996, 31 Suppl 9 p69-74,
ISSN 0944-1174 Journal Code: 9430794
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The initial steps have been taken towards the development of a vaccine against the human gastroduodenal pathogen, Helicobacter pylori. Proof of principle was achieved when mice were protected against challenge with living Helicobacter felis, a close relative of the human pathogen, following oral immunization with H . felis sonicate and the mucosal adjuvant, cholera toxin. Similar results with H . pylori antigen have allowed development of possible human vaccines . Recombinant urease protein has been proposed as a major vaccine candidate, together with

the heat-labile toxin of Escherichia coli as the adjuvant. Probably the most significant finding in the early vaccine studies was that immunization of already infected mice resulted in a cure of Helicobacter infection. The possibility of a therapeutic vaccine makes commercial development more attractive, as large populations could be immunized without the potential for development of drug-resistant strains that currently restricts widespread antibiotic use. For advanced societies with powerful economies yet a high prevalence of H . pylori, such as Japan, vaccine development should become a high national health priority.

6/AB/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09238083 97142160 PMID: 8988394
Cell envelope characteristics of Helicobacter pylori: their role in adherence to mucosal surfaces and virulence.
Clyne M; Drumm B
Department of Paediatrics, University College Dublin, Our Ladys Hospital for Sick Children, Crumlin, Ireland.
FEMS immunology and medical microbiology (NETHERLANDS) Dec 1 1996, 16 (2) p141-55, ISSN 0928-8244 Journal Code: 9315554
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Helicobacter pylori colonises the gastric mucosa of humans and causes both antral gastritis and duodenal ulcer disease. Exactly how H . pylori causes disease is not known but several pathogenic determinants have been proposed for the organism. These include adhesins, cytotoxins and a range of different enzymes including urease , catalase and superoxide dismutase. Surface molecules of H . pylori such as flagella, lipopolysaccharide, the urease enzyme and outer membrane proteins are putative adhesin molecules. While phosphatidylethanolamine and the Lewis(b) blood group antigen have been proposed as receptor molecules for the organism the exact mechanism by which H . pylori adheres to the gastric mucosa has still to be identified. Characterisation of the adhesins of H . pylori could lead to the development of adhesin analogues for use in the inhibition of colonisation and improved therapy for ulcer disease. In vivo studies with isogenic mutants which are incapable of adhering to the gastric mucosa would greatly clarify the significance of adherence. Such mutants could possibly be useful as a vaccine against infection with wild-type organisms.

6/AB/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09181330 97067620 PMID: 8911016
Helicobacter pylori and gastroduodenal disorders: new approaches for prevention, diagnosis and treatment.
Kotloff K L
Department of Pediatrics, University of Maryland School of Medicine, Baltimore 21201, USA.
Vaccine (ENGLAND) Aug 1996, 14 (12) p1174-5, ISSN 0264-410X Journal Code: 8406899
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Prevention and treatment of H . pylori infection through immunization

would be an important achievement considering the high cost of drug therapy, the appearance of antibiotic resistant strains, and the failure of drug therapy to prevent reinfection. Success hinges on determining the extent to which immunologic memory can be evoked in the stomach , and the ability to identify antigens and delivery systems which stimulate protective immunity rather than disease-promoting responses. Recent experiments by several groups have demonstrated that mice immunized orally or intragastrically (along with mucosal adjuvant) with whole H . pylori lysate, purified or recombinant urease , or purified VacA were significantly protected against challenge with virulent Helicobacter . Several vaccine candidates will enter clinical trials in humans in the near future.

6/AB/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08802740 96153005 PMID: 8563056
Animal models and vaccine development.
Lee A
School of Microbiology and Immunology, University of New South Wales, Kensington, Sydney, Australia.
Bailliere's clinical gastroenterology (ENGLAND) Sep 1995, 9 (3) p615-32, ISSN 0950-3528 Journal Code: 8704786
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Following the demonstration of Helicobacter pylori as a major gastroduodenal pathogen there was a need to develop animal models in order to investigate mechanisms of pathogenesis and to be able to test new treatment strategies. Helicobacter pylori will only colonize a limited number of hosts including non-human primates, germ-free or barrier raised piglets, germ-free dogs and recently laboratory raised cats. Although these models have proved useful there is a need for more convenient small animal models. The ferret infected with its natural gastric organism, Helicobacter mustelae, is the only other animal to show peptic ulceration and has been successfully used to investigate gastritis and antimicrobial agents. The other commonly used animal model is the laboratory mouse or rat infected with either Helicobacter felis or Helicobacter heilmannii, bacteria that normally colonize cat or dog gastric mucosae. Active/chronic gastritis , gastric atrophy, and lymphoma -like lesions have been shown to develop in H . felis infected mice. The most recent and exciting use of an animal model has been the use of the H . felis mouse model in the development of human vaccines against H . pylori. Mice can be protected against infection with large doses of viable H . felis by oral immunization using sonicates of H . felis or H . pylori or recombinant H . pylori urease together with cholera toxin or cholera toxin-B subunit as the mucosal adjuvant. More importantly it has been shown that immunization of already infected animals results in eradication of infection. This raises the intriguing possibility that therapeutic immunization might be a viable option in the management of Helicobacter -associated disease. If immunization as a therapy of peptic ulcers was combined with short-term acid suppression, the possibility of reinfection may also be eliminated. In those countries where H . pylori infection rates are very high and infection occurs at an early age, large scale oral immunization of sections of the community would not only protect the young from the deleterious consequences of long-term H . pylori infection but could also cure existing disease.

6/AB/13 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08761383 96100076 PMID: 8574728
Vaccine strategies for prevention of Helicobacter pylori infection.
Sellman S; Blanchard T G; Nedrud J G; Czinn S J
Department of Pediatrics, Case Western Reserve University, Cleveland, Ohio, USA.
European journal of gastroenterology & hepatology (ENGLAND) Aug 1995, 7 Suppl 1 pS1-6, ISSN 0954-691X Journal Code: 9000874
Contract/Grant No.: DK 46461; DK; NIDDK; HL-37117; HL; NHLBI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
OBJECTIVE: To examine the level and duration of the humoral immune response to Helicobacter felis following oral immunization or infection. DESIGN AND METHODS: Germ-free mice were orally immunized with sonicated H . felis plus cholera toxin five times over 6 weeks. One week after immunization was completed, immunized and control non-immunized mice received an oral challenge of live H . felis organisms. The animals were killed at 3-week intervals and serum, gastric washings, intestinal washings and gastric biopsies were obtained. H . felis infection was confirmed by a positive urease test or culture of the gastric biopsy. Serum gastric and intestinal antibody titers were determined by enzyme-linked immunosorbent assay. CONCLUSION: Infection and immunization against H . felis produces a specific humoral response. The humoral response in infection alone is significantly smaller than that of immunized animals until 6 weeks after infection. The humoral response following oral immunization persists for at least 18 weeks without further stimulation. The presence of an H . felis-specific antibody immune response before infection may be needed to protect animals from acute Helicobacter infection.

6/AB/14 (Item 14 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08569258 95327674 PMID: 7604021
The GroES homolog of Helicobacter pylori confers protective immunity against mucosal infection in mice.
Ferrero R L; Thiberge J M; Kansau I; Wuscher N; Huerre M; Labigne A
Unite des Enterobacteries, Institut National de la Sante et de la Recherche Medicle U389, Paris, France.
Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jul 3 1995, 92 (14) p6499-503, ISSN 0027-8424 Journal Code: 7505876
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Helicobacter pylori is an important etiologic agent of gastroduodenal disease. In common with other organisms, H . pylori bacteria express heat shock proteins that share homologies with the GroES-GroEL class of proteins from Escherichia coli. We have assessed the heat shock proteins of H . pylori as potential protective antigens in a murine model of gastric Helicobacter infection. Orogastric immunization of mice with recombinant H . pylori GroES- and GroEL-like proteins protected 80% (n = 20) and 70% (n = 10) of animals, respectively, from a challenge dose of 10(4) Helicobacter felis bacteria (compared to control mice, P = 0.0042 and P = 0.0904, respectively). All mice (n = 19) that were immunized with a dual

antigen preparation, consisting of H . pylori GroES-like protein and the B subunit of H . pylori urease , were protected against infection. This represented a level of protection equivalent to that provided by a sonicated Helicobacter extract (P = 0.955). Antibodies directed against the recombinant H . pylori antigens were predominantly of the IgG1 class, suggesting that a type 2 T-helper cell response was involved in protection. This work reports a protein belonging to the GroES class of heat shock proteins that was shown to induce protective immunity. In conclusion, GroES-like and urease B-subunit proteins have been identified as potential components of a future H . pylori subunit vaccine .

6/AB/15 (Item 15 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08561272 95318517 PMID: 7797906
Oral immunization with recombinant Helicobacter pylori urease induces secretory IgA antibodies and protects mice from challenge with Helicobacter felis.
Lee C K; Weltzin R; Thomas W D; Kleanthous H; Ermak T H; Soman G; Hill J E; Ackerman S K; Monath T P
OraVax, Inc., Cambridge, MA 02139, USA.
Journal of infectious diseases (UNITED STATES) Jul 1995, 172 (1) p161-72, ISSN 0022-1899 Journal Code: 0413675
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Helicobacter pylori, a gram-negative spiral bacterium, is the cause of chronic superficial (type B) gastritis and peptic ulcer disease. The urease enzyme of H . pylori was expressed as an inactive recombinant protein in Escherichia coli, purified as particulate structures of 550-600 kDa molecular mass with a diameter of approximately 12 nm. Given orally, 5 micrograms of urease with an appropriate mucosal adjuvant, such as the labile toxin of E. coli, protected 60%-100% of mice against challenge with virulent Helicobacter felis. Protection correlated with the level of secretory IgA antibodies against urease . Oral administration of antigen was as effective or better than intragastric administration. Parenteral injection of antigen or intragastric administration of high-dose antigen without adjuvant elicited serum IgG but no IgA antibodies and did not confer protection. Recombinant urease as an oral vaccine candidate deserves further investigation as an approach to the prevention of Helicobacter -induced chronic gastroduodenal diseases in humans.

6/AB/16 (Item 16 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08560401 95317528 PMID: 7797009
Oral immunization with Helicobacter pylori urease B subunit as a treatment against Helicobacter infection in mice.
Corthesy-Theulaz I; Porta N; Glauser M; Saraga E; Vaney A C; Haas R; Kraehenbuhl J P; Blum A L; Michetti P
Division of Gastroenterology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.
Gastroenterology (UNITED STATES) Jul 1995, 109 (1) p115-21, ISSN 0016-5085 Journal Code: 0374630
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

BACKGROUND & AIMS: Eradication of Helicobacter pylori infections in humans results in the healing of gastritis and gastric ulcers . This study used a mouse model to test whether oral vaccination can cure Helicobacter infection and gastritis . METHODS: Mice were infected with Helicobacter felis. Three weeks after infection, the mice were orally immunized with H . pylori urease B subunit. Control mice were simultaneously infected but sham immunized. RESULTS: Three to 8 weeks after oral immunization of H . felis-infected mice with recombinant H . pylori urease B subunit, the infection cleared and there was no evidence of gastritis . Vaccinated mice remained protected against two consecutive H . felis challenges. CONCLUSIONS: These results show that the lack of natural immunity against Helicobacter can be overcome by oral immunization and that vaccination offers a novel therapeutic approach to Helicobacter -induced gastritis .

6/AB/17 (Item 17 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08448748 95197244 PMID: 7890380
Effect of oral immunization with recombinant urease on murine Helicobacter felis gastritis .
Pappo J; Thomas W D; Kabok Z; Taylor N S; Murphy J C; Fox J G
Vaccine Delivery Research Section, OraVax Inc., Cambridge, Massachusetts 02139.
Infection and immunity (UNITED STATES) Apr 1995, 63 (4) p1246-52, ISSN 0019-9567 Journal Code: 0246127
Contract/Grant No.: 5-P01-CA26731; CA; NCI; AI34679; AI; NIAID; DK 36563; DK; NIDDK; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The ability of oral immunization to interfere with the establishment of infection with Helicobacter felis was examined. Groups of Swiss Webster mice were immunized orally with 250 micrograms of Helicobacter pylori recombinant urease (rUrease) and 10 micrograms of cholera toxin (CT) adjuvant, 1 mg of H . felis sonicate antigens and CT, or phosphate-buffered saline (PBS) and CT. Oral immunization with rUrease resulted in markedly elevated serum immunoglobulin G (IgG), serum IgA, and intestinal IgA antibody responses. Challenge with live H . felis further stimulated the urease -specific intestinal IgA and serum IgG and IgA antibody levels in mice previously immunized with rUrease but activated primarily the serum IgG compartment of PBS-treated and H . felis-immunized mice. Intestinal IgA and serum IgG and IgA anti- urease antibody responses were highest in rUrease-immunized mice at the termination of the experiment. Mice immunized with rUrease were significantly protected ($P <$ or $= 0.0476$) against infection when challenged with H . felis 2 or 6 weeks post-oral immunization in comparison with PBS-treated mice. Whereas H . felis-infected mice displayed multifocal gastric mucosal lymphoid follicles consisting of CD45R+ B cells surrounded by clusters of Thy1.2+ T cells, gastric tissue from rUrease-immunized mice contained few CD45R+ B cells and infrequent mucosal follicles. These observations show that oral immunization with rUrease confers protection against H . felis infection and suggest that gastric tissue may function as an effector organ of the mucosal immune system which reflects the extent of local antigenic stimulation.

6/AB/18 (Item 18 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08254207 95011230 PMID: 7926454
Immunization of BALB/c mice against Helicobacter felis infection with Helicobacter pylori urease.
Michetti P; Corthesy-Theulaz I; Davin C; Haas R; Vaney A C; Heitz M; Bille J; Kraehenbuhl J P; Saraga E; Blum A L
Division of Gastroenterology, Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland.
Gastroenterology (UNITED STATES) Oct 1994, 107 (4) p1002-11, ISSN 0016-5085 Journal Code: 0374630
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
BACKGROUND/AIMS: Because Helicobacter pylori is a potentially dangerous human pathogen, the protective potential of oral immunization with H . pylori urease and its subunits was evaluated in an animal model. METHODS: Mice were orally immunized with H . pylori sonicate, urease , or recombinant enzymatically inactive urease subunits and then challenged with Helicobacter felis. Control mice were sham-immunized. RESULTS: H . felis colonization was present 5 days after challenge in 9 of 10 sham-immunized, 6 of 9 sonicate-immunized, and 3 of 10 urease -immunized animals (P = 0.031 vs. sham-immunized). Twelve days after challenge, urease B-immunized mice had a weaker colonization than sham-immunized controls, whereas urease A had no effect. After 70 days, most urease A- and urease B-immunized mice had cleared the colonization (10/17: P = 0.0019; 16/20: P = 0.00002 vs. sham-immunized). In urease B-immunized animals, protection was often associated with corpus gastritis . CONCLUSIONS: Oral immunization with H . pylori urease protects mice against H . felis infection. Enzymatically inactive urease A and B subunits contain protective epitopes. It is unclear whether protection depends on the development of a mononuclear inflammatory response in the gastric corpus. Our observations should encourage the development of a human vaccine .

6/AB/19 (Item 19 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08121494 94237422 PMID: 8181696
Lack of protection against gastric Helicobacter infection following immunisation with jack bean urease : the rejection of a novel hypothesis.
Chen M; Lee A; Hazell S L; Hu P; Li Y
School of Microbiology and Immunology, University of New South Wales, Kensington, Australia.
FEMS microbiology letters (NETHERLANDS) Mar 1 1994, 116 (3) p245-50, ISSN 0378-1097 Journal Code: 7705721
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The common mucosal immune system was stimulated by oral immunisation with jack bean urease and the adjuvant cholera toxin. A high level of local antibody and serum antibody was induced in mice following hyperimmunisation with this combination. No cross-reacting antibody was found against either Helicobacter pylori or Helicobacter felis. No protection was observed against oral challenge of immunised mice with living H. felis thus disproving the interesting hypothesis of Pallen and Clayton that plant urease might induce a protective immunity against helicobacter infection.

6/AB/20 (Item 20 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08029016 94156469 PMID: 8112850
Immunological and molecular characterization of Helicobacter felis urease.
Gootz T D; Perez-Perez G I; Clancy J; Martin B A; Tait-Kamradt A; Blaser M J
Department of Immunology and Infectious Diseases, Central Research Division, Pfizer Inc., Groton, Connecticut 06340.
Infection and immunity (UNITED STATES) Mar 1994, 62 (3) p793-8, ISSN 0019-9567 Journal Code: 0246127
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

Urease activity has recently been shown to be an important virulence determinant for Helicobacter pylori, allowing it to survive the low pH of the stomach during colonization. Experimental murine infection with Helicobacter felis is now being used as a model for H . pylori infection to study the effects of vaccines , antibiotics, and urease inhibitors on colonization. However, little information comparing the ureases of H . felis and H . pylori is available. Urease was partially purified from the cell surface of H . felis ATCC 49179 by A-5M agarose chromatography, resulting in an eightfold increase in specific activity over that of crude urease . The apparent Km for urea for the partially purified urease was 0.4 mM, and the enzyme was inhibited in a competitive manner by flurofamide (50% inhibitory concentration = 0.12 microM). Antiserum to whole cells of H . pylori recognized both H . pylori and H . felis urease B subunits. Antiserum raised against H . felis whole cells recognized the large and small autologous urease subunits and the cpn60 heat shock molecule in both H . felis and H . pylori. However, this antiserum showed only a weak reaction with the B subunit of H . pylori urease . Two oligomeric DNA sequences were used as probes to evaluate the relatedness of H . felis and H . pylori urease gene sequences. One 30-mer from the ureA sequence, which had been shown previously to be specific for H . pylori, failed to hybridize to H . felis genomic DNA. A probe to the putative coding sequence for the active site of the H . pylori ureB subunit hybridized at low intensity to a 2.8-kb fragment of BamHI-HindIII-digested H . felis DNA, suggesting that the sequences were homologous but not identical, a result confirmed from the recently published sequences of ureA and ureB from H . felis.

6/AB/21 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12900306 BIOSIS NO.: 200100107455
Evaluation of factors that can affect protective immune responses following oral immunization of recombinant Helicobacter pylori urease apoenzyme.
AUTHOR: Kim Jang Seong; Chang Ji Hoon; Park Eun Jeong; Chung Soo Il; Yum Jung Sun(a)
AUTHOR ADDRESS: (a)Mogam Biotechnology Research Institute, 341 Pojung-Ri, Koosung-Myon, Yongin, Kyonggi-Do, 449-910: jsyum@greencross.com**South Korea
JOURNAL: Journal of Microbiology and Biotechnology 10 (6):p865-872 December, 2000
MEDIUM: print
ISSN: 1017-7825
DOCUMENT TYPE: Article

RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Helicobacter pylori is the major cause of gastritis , peptic ulcer , and a principal risk factor for gastric cancer. As the first step towards a vaccine against H . pylori infection, H . pylori urease was expressed and purified as a recombinant apoenzyme (rUrease) in E. coli. In order to develop an effective immunization protocol using rUrease, the host immune responses were evaluated after the oral immunization of mice with rUrease preparations plus cholera toxin relative to various conditions, such as the physical nature of the antigen, the frequency of the booster immunization, the dose of the antigen, and the route of administration. The protective efficacy was assessed using a quantitative culture following an H . pylori SS1 challenge. It was demonstrated that rUrease, due to its particulate nature, was more superior than the UreB subunit as a vaccine antigen. The oral immunization of rUrease elicited significant systemic and secretory antibody responses, and activated predominantly Th2-type cellular responses. The bacterial colonization was significantly reduced (apprx100-fold) in those mice immunized with three or four weekly oral doses of rUrease plus cholera toxin ($p<0.05$), when compared to the non-immunized/challenged controls. The protection correlated well with the elicited secretory IgA level against rUrease, and these secretory antibody responses were highly dependent on the frequency of the booster immunization, yet unaffected by the dose of the antigen (25-200 mug). These results demonstrate the remarkable potential of rUrease as a vaccine antigen, thereby strengthening the possibility of developing an H . pylori vaccine for humans.
2000

6/AB/22 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10769777 BIOSIS NO.: 199799390922
Resolution of gastritis and duration of protection against H . felis infection after oral immunization with recombinant urease .
AUTHOR: Ermak T H; Kleanthous H K; Myers G; Ding R; Lee C K; Pappo J; Monath T P
AUTHOR ADDRESS: OraVax Inc., Cambridge, MA**USA
JOURNAL: Gut 39 (SUPPL. 2):pA45 1996
CONFERENCE/MEETING: IXth International Workshop on Gastroduodenal Pathology and Helicobacter pylori Copenhagen, Denmark October 16-19, 1996
ISSN: 0017-5749
RECORD TYPE: Citation
LANGUAGE: English
1996

6/AB/23 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10699777 BIOSIS NO.: 199799320922
Immunomagnetic bead enrichment and PCR for detection of Helicobacter pylori in human stools.
AUTHOR: Nilsson Hans-Olof; Aleljung Par(a); Nilsson Ingrid; Tyszkiewicz Tadeusz; Wadstrom Torkel
AUTHOR ADDRESS: (a)Dep. Med. Microbiol., Univ. Lund, Solvegatan 23, S-223

62 Lund**Sweden
JOURNAL: Journal of Microbiological Methods 27 (1):p73-79 1996
ISSN: 0167-7012
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: An immunomagnetic bead-based polymerase chain reaction assay (IMS-PCR) was developed for the detection of Helicobacter pylori in experimentally inoculated human stools and human clinical stool samples. Magnetic beads coated with anti- H . pylori rabbit antibodies were used for enrichment and concentration of H . pylori from faecal samples. Taq polymerase inhibitors, found in human faeces, are efficiently removed by the immunomagnetic separation (IMS) and subsequent washing of the magnetic beads. Conditions of the assay were developed and optimised with faeces from a healthy, H . pylori seronegative, individual. Faeces was inoculated with serial dilutions of either the spiral or the coccoid form of H . pylori. These two morphologic forms could be detected at similar concentrations when inoculated in faeces using an optimised IMS-PCR method. In 1 g of faeces less than 2.5 times 10-4 H . plori cells were detected as measured with two separate sets of PCR-primers, based on a urease A subunit gene sequence and a genesequence encoding a 26 kDa surface protein of H . pylori. Previously no report has shown a sensitivity below 10-6 H . pylori in faeces PCR. Preliminary analysis of stool samples from 17 patients with symptoms of gastritis and esophagitis by IMS-PCR showed a good correlation with EIA-analysis of H . pylori serum-antibodies from these patients. The results indicate that H . pylori cells are shed in faeces of infected patients and that immunomagnetic bead PCR might be an appropriate method for clinical diagnosis and studies involving immunoprophylaxis, antibiotic treatment as well as vaccine candidates.

1996

6/AB/24 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10398311 BIOSIS NO.: 199699019456
Oral vaccination with recombinant urease reduces gastric Helicobacter pylori colonization in the cat.
AUTHOR: Batchelder M(a); Fox J G(a); Monath T; Yan L(a); Attardo L; Georgakopoulos K; Li X(a); Marini R(a); Shen Z(a); Pappo J; Lee C
AUTHOR ADDRESS: (a)Div. Comparative Med., Massachusetts Inst. Technol., Cambridge, MA**USA
JOURNAL: Gastroenterology 110 (4 SUPPL.):pA58 1996
CONFERENCE/MEETING: 96th Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week San Francisco, California, USA May 19-22, 1996
ISSN: 0016-5085
RECORD TYPE: Citation
LANGUAGE: English
1996

6/AB/25 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09827770 BIOSIS NO.: 199598282688
Helicobacter pylori and cancer prone lesions of the stomach.

AUTHOR: De Koster E; Buset M; Fernandes E; Deltenre M
AUTHOR ADDRESS: Brugmann Univ. Hosp.**Belgium
JOURNAL: Acta Endoscopica 25 (1):p33-44 1995
ISSN: 0240-642X
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: French; Non-English
SUMMARY LANGUAGE: French; English

ABSTRACT: Gastric cancer still is a major health problem, in spite of its declining incidence. Its histopathogenesis is described in the Correa model, where environmental influences cause the evolution from a normal stomach through superficial and atrophic gastritis to intestinal metaplasia , dysplasia, and finally carcinoma. Helicobacter pylori is the main causative agent of chronic active gastritis . As chronic atrophic gastritis progresses, the density of the bacteria diminishes, and in severe atrophic gastritis , only serum antibodies against H . pylori remain. The development of chronic atrophic gastritis is associated with the presence of H . pylori, high gastric juice pH, low gastric juice vitamin C, and low serum levels of beta-carotene. Intestinal metaplasia is likewise associated with H . pylori low intake and gastric juice levels of vitamin C, high gastric juice pH, and bile reflux. High rates of H . pylori prevalence can also be found in patients with dysplasia and early gastric cancer; the role of H . pylori in the diffuse type of early gastric cancer is debated. Mechanisms involved in carcinogenesis include H . pylori-induced inflammation, with increased gastric cell proliferation and mutagenic inflammatory products; H . pylori-enabled stimulation of gastric cell proliferation by salt; H . pylori-induced abolishment of the gastric vitamin C concentration mechanism; H . pylori urease -produced ammonia, which is able in itself to induce atrophy; and H . pylori toxin, which is important in gastric carcinogenesis for unknown reasons. It is unknown whether some of the precancerous lesions are reversible or preventable; H . pylori eradication in selected patients and population-based vaccination should be evaluated.

1995

6/AB/26 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09551987 BIOSIS NO.: 199598006905
Recombinant Antigens Prepared from the Urease Subunits of Helicobacter spp.: Evidence of Protection in a Mouse Model of Gastric Infection.
AUTHOR: Ferrero Richard L(a); Thiberge Jean-Michel; Huerre Michel; Labigne Agnes
AUTHOR ADDRESS: (a)Unite Enterobacteries, Inst. Pasteur, 28 du Rue Dr. Roux, Paris 75724**France
JOURNAL: Infection and Immunity 62 (11):p4981-4989 1994
ISSN: 0019-9567
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Urease is an important virulence factor for gastric Helicobacter spp. To elucidate the efficacy of individual urease subunits to act as mucosal immunogens, the genes encoding the respective urease subunits (UreA and UreB) of Helicobacter pylori and Helicobacter felis were cloned in an expression vector (pMAL) and

expressed in Escherichia coli cells as translational fusion proteins. The recombinant UreA and UreB proteins were purified by affinity and anion-exchange chromatography techniques and had predicted molecular masses of approximately 68 and 103 kDa, respectively. Western blotting (immunoblotting) studies indicated that the urease components of the fusion proteins were strongly immunogenic and were specifically recognized by polyclonal rabbit anti- Helicobacter sp. sera. The fusion proteins (50 mu-g) were used, in combination with a mucosal adjuvant (cholera toxin), to orogastrically immunize mice against H . felis infection. Gastric tissues from H . felis-challenged mice were assessed by the biopsy urease test and by histology. In mice immunized with recombinant H . felis UreB, 60% of animals (n = 7) were histologically negative for H . felis bacteria after challenge at 17 weeks. This compared with 25% (n = 8) for mice immunized with the heterologous H . pylori UreB antigen. Neither the homologous nor the heterologous UreA subunit elicited protective responses against H . felis infection in mice. The study demonstrated that a recombinant subunit antigen could induce an immunoprotective response against gastric Helicobacter infection.

1994

6/AB/27 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08686654 Genuine Article#: 317AT Number of References: 37
Title: Accuracy of C-13-urea breath test in clinical use for diagnosis of Helicobacter pylori infection (ABSTRACT AVAILABLE)
Author(s): Riepl RL (REPRINT) ; Folwaczny C; Otto B; Klauser A; Blendinger C; Wiebecke B; Konig A; Lehnert P; Heldwein W
Corporate Source: UNIV MUNICH,MED KLIN, KLINIKUM INNENSTADT, ZIEMSSENSTR 1/D-80336 MUNICH//GERMANY/ (REPRINT); UNIV MUNICH,INST PATHOL, KLINIKUM INNENSTADT/D-80336 MUNICH//GERMANY/; MAX VON PETTENKOFER INST,/D-8000 MUNICH//GERMANY/
Journal: ZEITSCHRIFT FUR GASTROENTEROLOGIE, 2000, V38, N1 (JAN), P13-19
ISSN: 0044-2771 Publication date: 20000100
Publisher: DEMETER VERLAG GEORG THIEME VERLAG, PETRA SCHLAGENHAUF, RUDIGERSTR 14, D-70469 STUTTGART, GERMANY
Language: English Document Type: ARTICLE
Abstract: The C-13-urea breath test (UBT) is a noninvasive test for diagnosis of Helicobacter pylori infection of gastric mucosa. The aim of this prospective study was to assess the accuracy of a simple UBT in clinical routine use.

Methods: The study population comprised of 100 patients (49 f, 51 m) requiring diagnostic upper CT endoscopy. One biopsy specimen was taken from the gastric anll urn, body and fundus, respectively, for standard histological examination and one additional, specimen from each location was transformed into transport medium for cultivation of H . pylori. After vaccination of the culture plates the biopsies were tested for urease activity (UAT). After recovery from endoscopy the patients had to pass an one liter endexspiratory breath sample before and 15 min after drinking 200 mi orange juice, pH 3.6, containing 75 mg of C-13-urea. (CO2)-C-13 was measured in the breath samples using isotope-selective nondispersive infrared spectrometry.

Results: Defining gold standard groups with all biopsy tests (from antrum and corpus) positive or negative die (CO2)-C-13 delta over baseline (DOB) cut-off level of UBT was set at 6.5 parts per thousand

in order to best discriminate positive from negative patients (ROC analysis). UBT was positive in 37% of all subjects. Taken UAT and histological examination together (positive when both tests were positive) UBT displayed a sensitivity of 92%, a specificity of 94%, a positive predictive value of 89%, and a negative predictive value of 94%. When including the results of culture sensitivity and negative predictive value reached almost 100%. The mean of the (CO2)-C-13-DOB values from H. pylori-positive duodenal or gastric ulcer patients did not differ from controls (H, pylori-positive patients without leasions). The (CO2)-C-13-DOB values of the ulcer group were correlated significantly with the active inflammatory component of gastritis in antrum, corpus, and fundus.

Conclusion: UBT with this setup detects H. pylori infection in clinical routine use with high accuracy. The increase of exhaled (CO3)-C-13 does not predict ulcer disease but reflects the de -gree of active inflammation of gastric mucosa.

6/AB/28 (Item 2 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08480768 Genuine Article#: 290JW Number of References: 23
Title: Development of a new method for the determination of immune responses in the human stomach (ABSTRACT AVAILABLE)
Author(s): Bergquist C; MattssonRydberg A; Lonroth H; Svennerholm AM (REPRINT)
Corporate Source: GOTHENBURG UNIV,DEPT MED MICROBIOL & IMMUNOL, GULDHEDSGATAN 10A/S-41346 GOTHENBURG//SWEDEN/ (REPRINT); GOTHENBURG UNIV,DEPT MED MICROBIOL & IMMUNOL/S-41346 GOTHENBURG//SWEDEN/; GOTHENBURG UNIV,DEPT SURG/S-41346 GOTHENBURG//SWEDEN/
Journal: JOURNAL OF IMMUNOLOGICAL METHODS, 2000, V234, N1-2 (FEB 3), P51-59
ISSN: 0022-1759 Publication date: 20000203
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
Language: English Document Type: ARTICLE
Abstract: The discovery of the gastric pathogen Helicobacter pylori has created a need for accurate methods to study immune responses locally in the human stomach . Therefore, we have developed a quick and easy method for extraction of antibodies from gastric biopsies using saponin and compared this method with the more laborious analysis of antibody-secreting cells (ASCs) from gastric biopsies. We have also analyzed the antibody content in gastric aspirates, saliva and plasma. There was a strong correlation between the total IgA levels in the biopsy extracts and the frequencies of IgA-secreting cells. In addition, the IgA and IgG levels against a H , pylori whole membrane preparation and purified urease in the biopsy extracts correlated well with the frequencies of specific IgA and IgG secreting cells. However, the antibody levels in gastric aspirates, saliva and plasma specimens did not correlate with the frequencies of corresponding ASC in the gastric biopsies. Thus, the saponin extraction method is suitable for monitoring local antibody responses in the stomach , while analyses of gastric aspirates, saliva or plasma are not appropriate for this purpose. (C) 2000 Elsevier Science B.V. All rights reserved.

6/AB/29 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

08296686 Genuine Article#: 268KH Number of References: 97
Title: Pathogenesis of Helicobacter pylori infection (ABSTRACT AVAILABLE)
Author(s): McGee DJ; Mobley HLT (REPRINT)
Corporate Source: UNIV MARYLAND,SCH MED, DEPT MICROBIOL & IMMUNOL, 655 W BALTIMORE ST/BALTIMORE//MD/21201 (REPRINT); UNIV MARYLAND,SCH MED, DEPT MICROBIOL & IMMUNOL/BALTIMORE//MD/21201
Journal: CURRENT OPINION IN GASTROENTEROLOGY, 2000, V16, N1 (JAN), P24-31
ISSN: 0267-1379 Publication date: 20000100
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621
Language: English Document Type: ARTICLE
Abstract: Helicobacter pylori, a gram-negative, microaerophilic, motile, spiral-shaped bacterium, has been established as the etiologic agent of gastritis and peptic ulcers and is a major risk factor for gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma (MALT). The ability of H . pylori to cause this spectrum of diseases depends on host, bacterial, and environmental factors. Bacterial factors critical for H . pylori colonization of the gastric mucosa include urease , flagella, adhesins, and delta-glutamyltranspeptidase. Lipopolysaccharide, urease , and vacuolating cytotoxin are among the factors that allow H . pylori to persist for decades and invoke an intense inflammatory response, leading to damaged host cells. Genes in the cag pathogenicity island also contribute to the inflammatory response by initiating a signal transduction cascade, resulting in interleukin-8 production. Proinflammatory cytokines and a Th-1 cytokine response further exacerbates the inflammation. Products of the enzymes nitric oxide synthase (iNOS) and cyclooxygenase may perturb the balance between gastric epithelial cell apoptosis (ulcer formation) and proliferation (cancer), The host Th-1 response and antibodies directed against H . pylori do not eliminate the organism, which presents challenges to vaccine development. Vaccines that include urease have shown some promise, but improved adjuvants and animal models should hasten progress in vaccine research. H . pylori is the most genetically diverse organism known, and the panmictic population structure may contribute to the varying ranges of disease severity produced by different strains. The complete genome sequence of two strains of H . pylori has propelled this field forward, and numerous groups are now using genomic, proteomic, and mutagenetic approaches to identify new virulence genes. Discovered only in 1982, H . pylori is now among the most intensely investigated organisms. This review summarizes recent progress in this rapidly moving field. (C) 2000 Lippincott Williams & Wilkins, Inc.

6/AB/30 (Item 4 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05464486 Genuine Article#: WA686 Number of References: 93
Title: HELICOBACTER-PYLORI - CAN THE MECHANISMS OF PATHOGENESIS GUIDE US TOWARDS NOVEL STRATEGIES FOR TREATMENT AND PREVENTION (Abstract Available)
Author(s): FALK P
Corporate Source: KAROLINSKA INST,DEPT MED,GASTROINTESTINAL RES LAB/S-17176 STOCKHOLM//SWEDEN/; WASHINGTON UNIV,SCH MED,DEPT MOL BIOL & PHARMACOL/ST LOUIS//MO/63110
Journal: JOURNAL OF INTERNAL MEDICINE, 1996, V240, N6 (DEC), P319-332
ISSN: 0954-6820
Language: ENGLISH Document Type: REVIEW
Abstract: Helicobacter pylori establishes a chronic infection in the stomach of humans. The infection is associated with a low grade

inflammatory response in the epithelium that can develop into chronic active gastritis , peptic ulcer disease or neoplasia. Antibiotics have dramatically decreased the rate of recurrence of peptic ulcers . However, antibiotic resistance is already evident, casting doubts on the future efficacy of these strategies. The link between childhood infection and severe health problems, including increased risk for gastric tumours motivate efforts to develop vaccines . Characterization of the molecular mechanisms of pathogenesis will pave the way for novel strategies for treatment and prevention of H. pylori infection.

6/AB/31 (Item 5 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05420678 Genuine Article#: VX237 Number of References: 43
Title: STRATEGIES FOR AN ORAL VACCINE AGAINST HELICOBACTER-PYLORI (Abstract Available)
Author(s): FERRERO RL; LABIGNE A
Corporate Source: INST PASTEUR,UNITE PATHOGENIE BACTERIENNE MUQUEUSES INSERM U38,28 RUE DR ROUX/F-75724 PARIS//FRANCE/
Journal: CURRENT OPINION IN GASTROENTEROLOGY, 1996, V12, N6 (NOV), P564-568
ISSN: 0267-1379
Language: ENGLISH Document Type: ARTICLE
Abstract: Helicobacter pylori is an etiologic agent of chronic gastritis , peptic ulcer disease, and gastric carcinogenesis in humans. Infection with H . pylori is common, with prevalence rates varying between 20% and 90%, depending on the population surveyed. Vigorous immune responses to H . pylori are observed in infected individuals, yet these responses are generally inadequate in eradicating the bacterium. Experiments in various animal models have established that immunization via the orogastric route can induce protective mucosal immune responses against gastric Helicobacter infections. Moreover, it was shown that active immunization could be used to eradicate an existent infection. Recently, several defined Helicobacter antigens were validated to be effective mucosal immunogens. One of these antigens (urease) has reached the clinical trial phase, Research toward the development of an H . pylori subunit vaccine has revealed that the stomach is a bona fide component of the common mucosal immune system.

6/AB/32 (Item 6 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05309200 Genuine Article#: VP428 Number of References: 46
Title: EFFECT OF GROWTH-PHASE AND ACID SHOCK ON HELICOBACTER-PYLORI CAGA EXPRESSION (Abstract Available)
Author(s): KARITA M; TUMMURU MKR; WIRTH HP; BLASER MJ
Corporate Source: VANDERBILT UNIV,SCH MED,DEPT MED,DIV INFECT DIS,A-3310 MED CTR N/NASHVILLE//TN/37232; VANDERBILT UNIV,SCH MED,DEPT MED,DIV INFECT DIS/NASHVILLE//TN/37232; DEPT VET AFFAIRS MED CTR,INFECT DIS SECT/NASHVILLE//TN/37212
Journal: INFECTION AND IMMUNITY, 1996, V64, N11 (NOV), P4501-4507
ISSN: 0019-9567
Language: ENGLISH Document Type: ARTICLE
Abstract: Helicobacter pylori strains possessing cagA are associated with peptic ulceration . To understand the regulation of expression of cagA, picB, associated with interleukin-8 induction, and ureA, encoding

the small urease subunit, we created gene fusions of cagA, ureA, and picB of strain 3401, using a promoterless reporter (xylE). Expression of XylE after growth in broth culture revealed that basal levels of expression of cagA and ureA in H . pylori were substantially greater than for picB. For cagA expression in stationary-phase cells, brief exposure to acid pH caused a significant increase in xylE expression compared with neutral pH. In contrast, expression of xylE in ureA or picB decreased after parallel exposure to acid pH (pH 7 > 6 > 5 > 4), regardless of the growth phase. Expression of the CagA protein varied with growth phase and pH exposure in parallel with the observed transcriptional variation, The concentration of CagA in a cell membrane-enriched fraction after growth at pH 6 was significantly higher than after growth at pH 5 or 7. We conclude that the promoterless reporter xylE is useful for studying the regulation of gene expression in H . pylori and that regulation of CagA production occurs mainly at the transcriptional level.

6/AB/33 (Item 7 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

05220676 Genuine Article#: VH958 Number of References: 68
Title: SOLITARY VIEWS OF THE STOMACH (Abstract Available)
Author(s): BLUM AL
Corporate Source: HOP CANTONAL UNIV GENEVA,DEPT MED INTERNE,DIV GASTROENTEROL/CH-1011 LAUSANNE//SWITZERLAND/
Journal: DIGESTION, 1996, V57, N5 (SEP), P287-298
ISSN: 0012-2823
Language: ENGLISH Document Type: ARTICLE
Abstract: Technology has propelled gastric physiology and pathophysiology since 1825, the year when the French Academy of Science tried to attribute a prize to the best paper on digestive physiology. I have analyzed the contributions of Ismar Boas, as well as my personal experience in studying gastric mucosal permeability, gastric secretion, a vaccine directed against Helicobacter pylori and the metabolism of this pathogen. In addition, I have examined the interplay between sociopolitical events and research activities, the role of suppressed minorities in research, the falacies of falsification strategies, the dependence of valid results from unorthodox experimental approaches and creative elements. Some of the older gastric researchers expressed solitary views - an attitude which may have helped them to make novel and valid observations.

6/AB/34 (Item 8 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04508786 Genuine Article#: TH574 Number of References: 27
Title: HELICOBACTER-PYLORI VACCINE - STATUS AND IMPLICATIONS FOR DRUG-THERAPY OF ULCER DISEASE (Abstract Available)
Author(s): CHEN MH
Corporate Source: SUN YAT SEN UNIV MED SCI,ZHONGSHAN RD 2/CANTON//PEOPLES R CHINA/
Journal: CLINICAL IMMUNOTHERAPEUTICS, 1995, V4, N6 (DEC), P420-424
ISSN: 1172-7039
Language: ENGLISH Document Type: ARTICLE
Abstract: Helicobacter pylori is now accepted aa the aetiological agent in peptic ulcer disease and has been characterised as a grade 1 carcinogen. The development of an effective vaccine is therefore

desirable, although effective therapies for the eradication of the organism are available. The first step towards the development of an anti- H . pylori vaccine was initiated by the demonstration that a sonicate of H . felis can protect mice against infection with H . felis. Urease has been identified in the mouse model as a protective antigen, Ether virulence factors, such as vacuolate cytotoxin and a heat shock protein of H . pylori, have been investigated as candidate vaccine components by the development of a new H . pylori mouse model. Vaccine adjuvants, delivery systems and therapeutic vaccination are likely to be the areas of major progress in the future.

6/AB/35 (Item 9 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04333162 Genuine Article#: RW006 Number of References: 37
Title: CONTRIBUTION OF UREASE TO ACID TOLERANCE IN YERSINIA-ENTEROCOLITICA (Abstract Available)
Author(s): DEKONINGWARD TF; ROBINSBROWNE RM
Corporate Source: ROYAL CHILDRENS HOSP,DEPT MICROBIOL & INFECT DIS,FLEMINGTON RD/PARKVILLE/VIC 3052/AUSTRALIA/; ROYAL CHILDRENS HOSP,DEPT MICROBIOL & INFECT DIS/PARKVILLE/VIC 3052/AUSTRALIA/; UNIV MELBOURNE,DEPT MICROBIOL/PARKVILLE/VIC 3052/AUSTRALIA/
Journal: INFECTION AND IMMUNITY, 1995, V63, N10 (OCT), P3790-3795
ISSN: 0019-9567
Language: ENGLISH Document Type: ARTICLE
Abstract: The stomach serves as a barrier to enteric infection because of the antibacterial effect of the hydrochloric acid in gastric juice. In this study, we tested the ability of the enteric pathogen Yersinia enterocolitica to tolerate a pH range of 2.0 to 6.0 and found that under the conditions of a normal human fasting stomach (pH < 3 and a gastric emptying time of 2 h), Y. enterocolitica is highly acid resistant, showing approximately 85% survival. The resistance of Y. enterocolitica to acid in vitro depended on the bacterial growth phase and the concentration of urea in the medium, being maximal during stationary phase in the presence of at least 0.3 mM urea. Urease -negative mutants of Y. enterocolitica were constructed by disrupting the urease gene complex of a virulent strain of serogroup O9. Compared with the wild type, these mutants shoved an approximately 1,000-fold decrease in the ability to tolerate acid in vitro (<0.08% survival) and a 10-fold reduction in viability after passage through the stomachs of mice. Complementation of the disrupted urease genes in trans restored the ability of urease -negative mutants to tolerate low pH in vitro and gastric acidity to approximately wild-type levels. These findings indicate that urease is responsible for acid resistance in Y. enterocolitica and suggest that urease contributes to the virulence of Y. enterocolitica by enhancing the likelihood of bacterial survival during passage through the stomach .

6/AB/36 (Item 10 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

03439567 Genuine Article#: PD890 Number of References: 52
Title: HELICOBACTER-PYLORI AND MOLECULAR-BIOLOGY - VIRULENCE FACTORS, DIAGNOSIS, AND VACCINE DEVELOPMENT (Abstract Available)
Author(s): SUERBAUM S
Corporate Source: RUHR UNIV BOCHUM,INST MED MIKROBIOL & IMMUNOL/D-44780

BOCHUM//GERMANY/
Journal: IMMUNITAT UND INFEKTION, 1994, V22, N4 (AUG), P137-141
ISSN: 0340-1162
Language: GERMAN Document Type: REVIEW
Abstract: The discovery of H.pylori as the etiologic agent of chronic antral type B gastritis and the finding that H.pylori is involved in the pathogenesis of gastroduodenal ulcer disease and gastric carcinoma have triggered intensive research about this organism. After overcoming considerable initial difficulties, researchers succeeded in adapting the instruments of molecular biology to the study of this highly fastidious organism. This has led to a rapid increase of knowledge concerning the basis of H.pylori virulence (as well as that of the related animal pathogens H.mustelae and H.felis) and to the development of molecular methods for the purposes of diagnosis and epidemiological research. The latest application of molecular biology in this area is the use of recombinant proteins for the development of an H.pylori vaccine . This review gives an overview of this rapidly developing field.

6/AB/37 (Item 11 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

02804182 Genuine Article#: ME638 Number of References: 0
(NO REFS KEYED)
Title: DEVELOPMENT OF A VACCINE AGAINST HELICOBACTER-PYLORI - A SHORT OVERVIEW (Abstract Available)
Author(s): RAPPUOLI R; BUGNOLI M; GHIARA P; COVACCI A; OLIVIERI R; XIANG ZY ; TELFORD JL
Corporate Source: IMMUNOBIOL RES INST SIENA,VIA FIORENTINA 1/I-53100 SIENA//ITALY/
Journal: EUROPEAN JOURNAL OF GASTROENTEROLOGY & HEPATOLOGY, 1993, V5, S2 (OCT), PS76-S78
ISSN: 0954-691X
Language: ENGLISH Document Type: ARTICLE
Abstract: Aim: Growing evidence that gastric and duodenal disease is caused by Helicobacter pylori infection suggests that this disease may be prevented by vaccination . We therefore assessed the possibilities for development of a vaccine .

Method: Survey of published studies.

Present state of development: Development of a vaccine requires identification of the factors responsible for bacterial virulence and disease induction and large-scale production and testing of potential vaccines in animal models. So far several factors involved in bacterial adhesion, colonization and virulence have been identified. Among these, the most promising candidates for vaccine development are the adhesins, the vacuolating cytotoxin and urease. Urease-based vaccines have shown some promising results in protecting mice against H. felis infection.

Proposals: The unique features of H. pylori infection and disease formation in man suggest that vaccines should be tested in models more relevant to humans, and that the vacuolating cytotoxin and the cytotoxin-associated gene A (cagA) should be seriously considered as vaccine candidates. This hypothesis is supported by the recent observation that only the subset of strains that produce the vacuolating cytotoxin and cagA are associated with disease.

6/AB/38 (Item 12 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

00858085 Genuine Article#: FB988 Number of References: 51
Title: SHUTTLE CLONING AND NUCLEOTIDE-SEQUENCES OF HELICOBACTER-PYLORI GENES RESPONSIBLE FOR UREASE ACTIVITY (Abstract Available)
Author(s): LABIGNE A; CUSSAC V; COURCOUX P
Corporate Source: INST PASTEUR,INSERM,UNITE ENTEROBACTERIES,U199/F-75724 PARIS 15//FRANCE/
Journal: JOURNAL OF BACTERIOLOGY, 1991, V173, N6, P1920-1931
Language: ENGLISH Document Type: ARTICLE
Abstract: Production of a potent urease has been described as a trait common to all Helicobacter pylori so far isolated from humans with gastritis as well as peptic ulceration . The detection of urease activity from genes cloned from H . pylori was made possible by use of a shuttle cosmid vector, allowing replication and movement of cloned DNA sequences in either Escherichia coli or Campylobacter jejuni. With this approach, we cloned a 44-kb portion of H . pylori chromosomal DNA which did not lead to urease activity when introduced into E. coli but permitted, although temporarily, biosynthesis of the urease when transferred by conjugation to C. jejuni. The recombinant cosmid (pILL585) expressing the urease phenotype was mapped and used to subclone an 8.1-kb fragment (pILL590) able to confer the same property to C. jejuni recipient strains. By a series of deletions and subclonings, the urease genes were localized to a 4.2-kb region of DNA and were sequenced by the dideoxy method. Four open reading frames were found, encoding polypeptides with predicted molecular weights of 26,500 (ureA), 61,600 (ureB), 49,200 (ureC), and 15,000 (ureD). The predicted UreA and UreB polypeptides correspond to the two structural subunits of the urease enzyme; they exhibit a high degree of homology with the three structural subunits of Proteus mirabilis (56% exact matches) as well as with the unique structural subunit of jack bean urease (55.5% exact matches). Although the UreD-predicted polypeptide has domains relevant to transmembrane proteins, no precise role could be attributed to this polypeptide or to the UreC polypeptide, which both mapped to a DNA sequence shown to be required to confer urease activity to a C. jejuni recipient strain.

6/AB/39 (Item 1 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

01396664 2000072798
Pilot study of phoP/phoQ-deleted Salmonella enterica serovar typhimurium expressing Helicobacter priori urease in adult volunteers
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ADDRESS: E.L. Hohmann, Infectious Diseases Division, Gray/Jackson 504, Department of Medicine, Boston, MA 02114, United States
EMAIL: ehohmann@partners.org
Journal: Infection and Immunity, 68/4 (2135-2141), 2000, United States
CODEN: INFIB
ISSN: 0019-9567
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English
NO. OF REFERENCES: 30

Attenuated Salmonella enterica serovar Typhi has been studied as an oral vaccine vector. Despite success with attenuated S. enterica serovar Typhimurium vectors in animals, early clinical trials of S. enterica

serovar Typhi expressing heterologous antigens have shown that few subjects have detectable immune responses to vectored antigens. A previous clinical study of phoP/phoQ-deleted S. enterica serovar Typhi expressing Helicobacter pylori urease from a multicopy plasmid showed that none of eight subjects had detectable immune responses to the vectored antigen. In an attempt to further define the variables important for engendering immune responses to vectored antigens in humans, six volunteers were inoculated with 5 x 10sup 7 to 8 x 10sup 7 CFU of phoP/phoQ-deleted S. enterica serovar Typhimurium expressing the same antigen. Two of the six volunteers had fever; none had diarrhea, bacteremia, or other serious side effects. The volunteers were more durably colonized than in previous studies of phoP/phoQ-deleted S. enterica serovar Typhi. Five of the six volunteers seroconverted to S. enterica serovar Typhimurium antigens and had strong evidence of anti-Salmonella mucosal immune responses by enzyme-linked immunospot studies. Three of six (three of five who seroconverted to Salmonella) had immune responses in the most sensitive assay of urease -specific immunoglobulin production by blood mononuclear cells in vitro. One of these had a fourfold or greater increase in end-point immunoglobulin titer in serum versus urease . Attenuated S. enterica serovar Typhimurium appears to be more effective than S. enterica serovar Typhi for engendering immune responses to urease . Data suggest that this may be related to a greater stability of antigen-expressing plasmid in S. enterica serovar Typhimurium and/or prolonged intestinal colonization. Specific factors unique to nontyphoidal salmonellae may also be important for stimulation of the gastrointestinal immune system.

6/AB/40 (Item 2 from file: 71)
DIALOG(R)File 71:ELSEVIER BIOBASE

00439042 96132926
Immunogenicity and safety of recombinant Helicobacter pylori urease in a nonhumnan primate
Stadtlander C.T.K.-H.; Gangemi J.D.; Khanolkar S.S.; Kitsos C.M.; Farris H.E. Jr.; Fulton L.K.; Hill J.E.; Huntington F.K.; Lee C.K.; Monath T.P.
ADDRESS: Dr. C.T.K.-H. Stadtlander, Greenville Hospital System, Clemson Unive. Biomed. Cooperative, Box 34 19 12, Clemson, SC 29634-1912, United States
Journal: Digestive Diseases and Sciences, 41/9 (1853-1862), 1996, United States
PUBLICATION DATE: 19960000
CODEN: DDSCD
ISSN: 0163-2116
DOCUMENT TYPE: Article
LANGUAGES: English SUMMARY LANGUAGES: English

Groups of squirrel monkeys (Saimiri spp.), predetermined to be free of Helicobacter infections in the gastric mucosa, were immunized orally with 0.5-4.5 mg of Helicobacter pylori recombinant urease (rUrease) and 25-500 mug of Escherichia coli heat-labile enterotoxin (LT) adjuvant. Oral immunization with rUrease resulted in a markedly elevated serum immunoglobulin G (IgG) antibody response with peak levels at 45 days after immunization. No significant gastric inflammation or cytotoxicity was evident in rUrease immunized monkeys as determined by light and electron microscopy. Twenty-five micrograms of LT was a sufficient and safe adjuvant dosage, whereas higher dosages resulted in diarrhea and lethargy. Animals developed a serum IgG antibody response to LT that did not impede the production of anti-rUrease antibody levels. The results of this investigation indicate that rUrease is immunogenic in a nonhuman primate.

6/AB/41 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

10583238 EMBASE No: 2000048045
Accuracy of sup 1sup 3C-urea breath test in clinical use for diagnosis of Helicobacter pylori infection
Riepl R.L.; Folwaczny C.; Otto B.; Klauser A.; Blendinger C.; Wiebecke B.; Konig A.; Lehnert P.; Heldwein W.
Dr. R.L. Riepl, Medizinische Klinik, Klinikum Innenstadt, Ludwig Maximilians-Univ. Munchen, Ziemssenstrasse 1, D-80336 Munchen Germany
Zeitschrift fur Gastroenterologie (Z. GASTROENTEROL.) (Germany) 2000, 38/1 (13-19)
CODEN: ZGASA ISSN: 0044-2771
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH; GERMAN
NUMBER OF REFERENCES: 37

The sup 1sup 3-urea breath test (UBT) is a noninvasive test for diagnosis of Helicobacter pylori infection of gastric mucosa. The aim of this prospective study was to assess the accuracy of a simple UBT in clinical routine use. Methods: The study population comprised of 100 patients (49 f, 51 m) requiring diagnostic upper GI endoscopy. One biopsy specimen was taken from the gastric antrum, body and fundus, respectively, for standard histological examination and one additional specimen from each location was transformed into transport medium for cultivation of H . pylori. After vaccination of the culture plates the biopsies were tested for urease activity (UAT). After recovery from endoscopy the patients had to pass an one liter endexspiratory breath sample before and 15 min after drinking 200 ml orange juice, pH 3.6. containing 75 mg of sup 1sup 3C-urea. sup 1sup 3COinf 2 was measured in the breath samples using isotope-selective nondispersive infrared spectrometry. Results: Defining gold standard groups with all biopsy tests (from antrum and corpus) positive or negative the sup 1sup 3COinf 2 delta over baseline (DOB) cut-off level of UBT was set at 6.5% in order to best discriminate positive from negative patients (ROC analysis). UBT was positive in 37% of all subjects. Taken UAT and histological examination together (positive when both tests were positive) UBT displayed a sensitivity of 92%, a specificity of 94%, a positive predictive value of 89%, and a negative predictive value of 94%. When including the results of culture sensitivity and negative predictive value reached almost 100%. The mean of the sup 1sup 3COinf 2-DOB values from H . pylori-positive duodenal or gastric ulcer patients did not differ from controls (H . pylori-positive patients without leasions). The sup 1sup 3COinf 2-DOB values of the ulcer group were correlated significantly with the active inflammatory component of gastritis in antrum, corpus, and fundus. Conclusion: UBT with this setup detects H . pylori infection in clinical routine use with high accuracy. The increase of exhaled sup 1sup 3COinf 2 does not predict ulcer disease but reflects the degree of active inflammation of gastric mucosa.

6/AB/42 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

06577958 EMBASE No: 1996242531
Prospects for improved therapy for Helicobacter pylori infection
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Clinical Sciences Building, Department of Medicine, Nepean Hospital, PO Box 63,Penrith, NSW 2751 Australia

Expert Opinion on Investigational Drugs (EXPERT OPIN. INVEST. DRUGS) (United Kingdom) 1996, 5/8 (959-976)
CODEN: EOIDE ISSN: 1354-3784
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Cure of Helicobacter pylori infection has been recommended for patients with peptic ulcer disease. However, an optimal treatment regimen has not been defined. Dual therapy regimens with omeprazole and amoxycillin or clarithromycin usually achieve eradication rates of 70-80%, while a combination of ranitidine bismuth citrate and clarithromycin produces eradication rates of over 80%. Triple therapy with a bismuth salt plus metronidazole and tetracycline or amoxycillin (the standard bismuth-based triple therapy), or a proton pump inhibitor (PPI-based therapy) plus two antimicrobial agents (metronidazole, amoxicillin or clarithromycin) is effective in eradicating H . pylori, with eradication rates of over 90% for metronidazole-sensitive strains. Drug resistance and compliance influence the clinical efficacy. Addition of a PPI to bismuth-based triple therapy (quadruple therapy) may overcome drug resistance, reduce side-effects, and shorten the treatment duration, but compliance may be reduced. Therefore, the search for a simple and effective therapy continues. Novel approaches include alternative types of drug administration (topical or parenteral), substitution with more powerful analogues or novel agents such as enzyme-inhibitors, Chinese herbs, honey, lactic acid and unsaturated fatty acids. Recently, vaccines against H . pylori infection have been developed and tested in animal models. The studies have demonstrated that oral immunisation with H . pylori whole cell sonicates or recombinant urease of the organism not only prevents the infection but can also eradicate it. Thus, therapeutic vaccines , which We believe are achievable, may finally eliminate H . pylori from the human stomach , and therefore cure most peptic ulcer disease.

6/AB/43 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

06133473 EMBASE No: 1995165582
Adjuvant therapy for Helicobacter pylori eradication: Role of lansoprazole shown in vitro

Megraud F.
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Journal of Clinical Gastroenterology (J. CLIN. GASTROENTEROL.) (United States) 1995, 20/SUPPL. 1 (S24-S27)
CODEN: JCGAD ISSN: 0192-0790
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The recognition of Helicobacter pylori (H . Pylori) as a major cause of gastroduodenal diseases has led to the use of antibiotics to treat these diseases. However, antibiotics used alone are not very effective, and adjuvant therapy is required. The most potent adjuvant therapy consists of increasing the stomach pH with proton pump inhibitors (PPIs). In addition to this action on stomach pH, PPIs, and especially lansoprazole, have been found to have antimicrobial activity against H . pylori. At high concentrations, they are even bactericidal. Furthermore, they can inhibit H . pylori urease activity. These properties, as well as their antisecretory activity, provide the grounds for their use in eradication of H . pylori.

6/AB/44 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

06005668 EMBASE No: 1995034320
An update on Helicobacter pylori
Wadstrom T.
Department of Medical Microbiology, Lund University, Solvegatan 23,S-223 62 Lund Sweden
Current Opinion in Gastroenterology (CURR. OPIN. GASTROENTEROL.) (United Kingdom) 1995, 11/1 (69-75)
CODEN: COGAE ISSN: 0267-1379
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Because of the limitations of animal models and the question of relevance of various in vitro observations, much controversy remains about the pathogenic mechanisms by which Helicobacter pylori can induce disease. Like those of other bacterial pathogens, the putative virulence factors of H . pylori can be divided into three groups: colonization factors, disease-inducing factors, and factors promoting persistence. Colonization factors allow the pathogen to become established in the host and include motility, urease production, and adhesion mechanisms. Disease-inducing factors consist of cytotoxins and urease , disruption of the gastric mucosal barrier, induction of inflammatory mediators, production of changed gastric physiology and possibly strain specific ulcerogenic properties. Finally, the importance of H . pylori infection may be due to its capacity for long-term persistence. An H . pylori infection can be considered a slow adaptive process. The mechanisms by which this pathogen survives and interacts with the host immune system may provide a model for other persistent mucosal pathogens. Eradication of H . pylori is now accepted therapy for peptic ulcer and may lead to elimination of a major risk factor for gastric malignancies.

6/AB/45 (Item 1 from file: 76)
DIALOG(R)File 76:Life Sciences Collection

01887667 3693842
The new path to preventing ulcers
Tompkins, L.S.; Falkow, S.
SCIENCE (WASH.) vol. 267, no. 5204, pp. 1621-1622 (1995)
ISSN: 0036-8075
DOCUMENT TYPE: Journal article LANGUAGE: ENGLISH
SUBFILE: Microbiology Abstracts B: Bacteriology; Medical and Pharmaceutical Biotechnology Abstracts

The close relation between Helicobacter infection, ulcers , and now stomach cancers has been ratified by a select panel of the National Institutes of Health. Helicobacter pylori is now on the list of microbial agents that are classified as carcinogens because of its close association with two types of gastric cancers. Infection of the stomach with H . pylori can occur as early as infancy. The research group reporting the new mouse model previously treated mice acutely with H . pylori to examine the role of VacA- and CagA-associated factors in the pathogenesis of the disease. Mice orally immunized with Helicobacter antigens, including VacA and urease , were protected from subsequent challenge with viable type I H . pylori strains. These results suggest not only that vaccination might indeed prevent Helicobacter infection, but also that it provides a

relatively cheap and simple model to identify other factors, including the CagA-associated gene products, that may be useful as vaccine antigens.

6/AB/46 (Item 1 from file: 144)
DIALOG(R)File 144:Pascal

14955955 PASCAL No.: 01-0108387
Evaluation of factors that can affect protective immune responses following oral immunization of recombinant Helicobacter pylori urease apoenzyme
JANG SEONG KIM; JI HOON CHANG; EUN JEONG PARK; SOO IL CHUNG; JUNG SUN YUM
Mogam Biotechnology Research Institute, 341 Pojung-Ri, Koosung-Myon, Yongin, Kyonggi-Do 449-910, Korea, Republic of
Journal: Journal of microbiology and biotechnology, 2000, 10 (6) 865-872
Language: English
Helicobacter pylori is the major cause of gastritis , peptic ulcer , and a principal risk factor for gastric cancer. As the first step towards a vaccine against H . pylori infection, H . pylori urease was expressed and purified as a recombinant apoenzyme (rUrease) in E. coli. In order to develop an effective immunization protocol using rUrease, the host immune responses were evaluated after the oral immunization of mice with rUrease preparations plus cholera toxin relative to various conditions, such as the physical nature of the antigen, the frequency of the booster immunization, the dose of the antigen, and the route of administration. The protective efficacy was assessed using a quantitative culture following an H . pylori SS1 challenge. It was demonstrated that rUrease, due to its particulate nature, was more superior than the UreB subunit as a vaccine antigen. The oral immunization of rUrease elicited significant systemic and secretory antibody responses, and activated predominantly Th2-type cellular responses. The bacterial colonization was significantly reduced (similar 100-fold) in those mice immunized with three or four weekly oral doses of rUrease plus cholera toxin ($p<0.05$), when compared to the non-immunized/challenged controls. The protection correlated well with the elicited secretory IgA level against rUrease, and these secretory antibody responses were highly dependent on the frequency of the booster immunization, yet unaffected by the dose of the antigen (25-200 mu g). These results demonstrate the remarkable potential of rUrease as a vaccine antigen, thereby strengthening the possibility of developing an H . pylori vaccine for humans.

6/AB/47 (Item 2 from file: 144)
DIALOG(R)File 144:Pascal

14653147 PASCAL No.: 00-0325168
Accuracy of SUP 1 SUP 3 C-urea breath test in clinical use for diagnosis of Helicobacter pylori infection
RIEPL R L; FOLWACZNY C; OTTO B; KLAUSER A; BLENDINGER C; WIEBECKE B; KOENIG A; LEHNERT P; HELDWEIN W
Medizinische Klinik, Klinikum Innenstadt, Ludwig-Maximilians-Universitaet Muenchen, Muenchen, Germany; Pathologisches Institut, Klinikum Innenstadt, Ludwig-Maximilians-Universitaet Muenchen, Muenchen, Germany; Max-von-Pettenkofer-Institut, Muenchen, Germany
Journal: Zeitschrift fuer Gastroenterologie, 2000, 38 (1) 13-19
Language: English Summary Language: German
The SUP 1 SUP 3 C-urea breath test (UBT) is a noninvasive test for

diagnosis of Helicobacter pylori infection of gastric mucosa. The aim of this prospective study was to assess the accuracy of a simple UBT in clinical routine use. Methods: The study population comprised of 100 patients (49 f, 51 m) requiring diagnostic upper GI endoscopy. One biopsy specimen was taken from the gastric antrum, body and fundus, respectively, for standard histological examination and one additional specimen from each location was transformed into transport medium for cultivation of H . pylori. After vaccination of the culture plates the biopsies were tested for urease activity (UAT). After recovery from endoscopy the patients had to pass an one liter endexspiratory breath sample before and 15 min alter drinking 200 ml orange juice, pH 3.6, containing 75 mg of SUP 1 SUP 3 C-urea. SUP 1 SUP 3 CO SUB 2 was measured in the breath samples using isotope-selective nondispersive infrared spectrometry. Results: Defining gold standard groups with all biopsy tests (from antrum and corpus) positive or negative the SUP 1 SUP 3 CO SUB 2 delta over baseline (DOB) cut-off level of UBT was set at 6.5& in order to best discriminate positive from negative patients (ROC analysis). UBT was positive in 37% of all subjects. Taken UAT and histological examination together (positive when both tests were positive) UBT displayed a sensitivity of 92%, a specificity of 94%, a positive predictive value of 89%, and a negative predictive value of 94%. When including the results of culture sensitivity and negative predictive value reached almost 100%. The mean of the SUP 1 SUP 3 CO SUB 2 -DOB values from H . pylori-positive duodenal or gastric ulcer patients did not differ from controls (H . pylori-positive patients without leasions). The SUP 1 SUP 3 CO SUB 2 -DOB values of the ulcer group were correlated significantly with the active inflammatory component of gastritis in antrum, corpus, and fundus. Conclusion; UBT with this setup detects H . pylori infection in clinical routine use with high accuracy. The increase of exhaled SUP 1 SUP 3 CO SUB 2 does not predict ulcer disease but reflects the degree of active inflammation of gastric mucosa.

6/AB/48 (Item 3 from file: 144)
DIALOG(R)File 144:Pascal

13167943 PASCAL No.: 97-0429764
Proprietes fonctionnelles et immunologiques de la chaperonine HspA de Helicobacter pylori
(Immunological and functional properties of the chaperonin HspA of helicobacter pylori)
KANSAU SILVA Imad Nasib; LABIGNE A, dir
Universite de Paris 07, Paris, Francee
Univ.: Universite de Paris 07. Paris. FRA Degree: Th. doct.
1996-07; 1996 256 p.
Language: French Summary Language: French; English
Helicobacter pylori est une bacterie responsable de gastrites chroniques qui peuvent evoluer vers la maladie ulcereuse , l'atrophie gastrique et les carcinomes gastriques . L'objectif de ce travail a ete de caracteriser la chaperonine HspA (homologue a GroES) de H . pylori sur le plan genetique, moleculaire et immunologique. La caracterisation de l'operon codant pour HspA et HspB (homologue a GroEL) a revele une organisation similaire a celle des operons groESL d'autres bacteries. HspA s'est averee unique du fait de la presence, dans sa partie C-terminale, d'une sequence riche en residus histidine. La construction de proteines recombinantes contenant differents fragments de HspA fusionnes a la proteine MBP et l'etude de leur affinite pour divers cations divalents ont permis de demontrer que HspA presente une plus forte affinite pour les ions nickel que pour les autres cations ; la fixation du nickel a lieu sur la

partie C-terminale de HspA. La co-expression du gene hspA et des genes ureasiques de H . pylori chez Escherichia coli a confirme le role de HspA dans l'activation de l' urease . Par ailleurs, il a ete montre que HspA est immunogene et que la reponse serique des patients infectes est dirigee principalement contre sa partie N-terminale. Neanmoins, seule une partie des patients infectes produit des anticorps anti-HspA. L'analyse de la sequence en acides amines de la proteine codee par des isolats cliniques a revele l'existence de deux variants antigeniques. Cependant, aucune correlation n'a pu etre observee entre la presence de chacun de ces variants et la production d'anticorps. Enfin, dans un modele murin, HspA augmente les proprietes protectrices de la fraction UreB de la preparation vaccinale . L'ensemble des donnees acquises a permis d'esquisser un premier modele fonctionnel du role de HspA vis-a-vis de l' urease . Les donnees immunologiques presentees ouvrent des perspectives pour la recherche des moyens de protection contre l'infection a H . pylori

6/AB/49 (Item 4 from file: 144)
DIALOG(R)File 144:Pascal

12619005 PASCAL No.: 96-0308028
Therapeutic immunization against Helicobacter mustelae in naturally infected ferrets
CUENCA R; BLANCHARD T G; CZNN S J; NEDRUD J G; MONATH T P; LEE C K; REDLINE R W
Department of Pediatrics, Case Western Reserve University, Cleveland, Ohio, United States
Journal: Gastroenterology : (New York, NY. 1943), 1996, 110 (6) 1770-1775
Language: English
Background & Aims : Helicobacter infection of the gastric antrum is responsible for a number of gastric disorders. Antibiotic therapy is lengthy and is not always effective. It has been shown previously that oral immunization against Helicobacter felis in mice can prevent colonization after challenge. The aim of this study was to investigate the efficacy of therapeutic immunization in eradicating an established Helicobacter infection and in reducing gastritis . Methods : Domestic ferrets, confirmed to be infected with Helicobacter mustelae by gastric endoscopy, were orally immunized with varying doses of purified Helicobacter pylori urease in combination with the mucosal adjuvant cholera toxin. Ferrets were assessed 1 week and 6 weeks after treatment for infection and pathology. Results : Therapeutic immunization eradicated Helicobactercolonization in 30% of all immunized ferrets, although there was no difference in efficacy between the varying doses of antigen tested. The difference was statistically significant when compared with animals administered cholera toxin alone or buffer (P = 0.04). The intensity of inflammation was also significantly reduced In immunized animals (P = 0.0003). Conclusions : Oral immunization with purified H . pylori urease and cholera toxin can eradicate H . mustelae in a natural host pathogen model. Oral immunization of chronically infected animals markedly reduced gastric inflammation.

6/AB/50 (Item 5 from file: 144)
DIALOG(R)File 144:Pascal

12313354 PASCAL No.: 95-0550809

Vaccine strategies for prevention fo helicobacter pylori infection
SELLMAN S; BLANCHARD T G; NEDRUD J G; CZINN S J
AXON Anthony T R, ed; BLASER M J, ed; KIMURA Ken, ed; MEGRAUD Francis, ed ; SHIMOYAMA Takashi, ed; SIPPONEN P, ed; WYLE F A, ed
Case western reserve univ., dep. pediatrics, Cleveland OH 44106, USA
General infirmary, cent. digestive diseases, Leeds, United Kingdom; Groupe hosp. Pellegrin, lab. bacteriologie enfants, 33076 Bordeaux, France
International symposium on Helicobacter pylori and its diseases, 7 (Tokyo JPN) 1994-04-18
Journal: European journal of gastroenterology & hepatology, 1995, 7 (SUP1) S1-S6
Language: English
Objectives: To examine the level and duration of the humoral immune response to Helicobacter felis following oral immunization or infection. Design and methods: Germ-free mice were orally immunized with sonicated H . felis plus cholera toxin five times over 6 weeks. One week after immunization was completed, immunized and control non-immunized mice received an oral challenge of live H . felis organisms. The animals were killed at 3-week intervals and serum, gastric washings, intestinal washings and gastric biopsies were obtained. H . felis infection was confirmed by a positive urease test or culture of the gastric biopsy. Serum gastric and intestinal antibody titers were determined by enzyme-linked immunosorbent assay. Conclusion: Infection and immunization against H . felis produces a specific humoral response. The humoral response in infection alone is significantly smaller than that of immunized animals until 6 weeks after infection. The humoral response following oral immunization persists for at least 18 weeks without further stimulation. The presence of an H . felis-specific antibody immune response before infection may be needed to protect animals from acute Helicobacter infection.

6/AB/51 (Item 6 from file: 144)
DIALOG(R)File 144:Pascal

11491518 PASCAL No.: 94-0329560
Lack of protection against gastric helicobacter infection following immunisation with jack bean urease : the rejection of a novel hypothesis
MINHU CHEN; LEE A; HAZELL S L; PINJIN HU; YIYANG LI
Univ. New South Wales, school microbiology immunology, Kensington N.S.W. 2033, Australia
Journal: FEMS microbiology letters, 1994, 116 (3) 245-250
Language: English

6/AB/52 (Item 1 from file: 351)
DIALOG(R)File 351:Derwent WPI

013515584
WPI Acc No: 2000-687530/200067
XRAM Acc No: C00-209315
Product comprising a synergistic combination of HpaA and HOP38 polypeptides, or fusion polypeptides, useful for treating or reducing the risk of Helicobacter pylori infection
Patent Assignee: ASTRAZENECA AB (ASTR)
Inventor: PAPPO J
Number of Countries: 092 Number of Patents: 002
Patent Family:
Patent No Kind Date Applicat No Kind Date Week

WO 200066624 A1 20001109 WO 2000SE808 A 20000428 200067 B
AU 200047894 A 20001117 AU 200047894 A 20000428 200111

Priority Applications (No Type Date): SE 991548 A 19990429
Patent Details:
Patent No Kind Lan Pg Main IPC Filing Notes
WO 200066624 A1 E 65 C07K-014/205
Designated States (National): AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
AU 200047894 A C07K-014/205 Based on patent WO 200066624

Abstract (Basic): WO 200066624 A1
Abstract (Basic):

NOVELTY - A pharmaceutical product comprising polypeptides for simultaneous or sequential administration to a mammal for preventing or treating Helicobacter pyroli infection, is new.

DETAILED DESCRIPTION - A pharmaceutical product comprising polypeptides for simultaneous or sequential administration to a mammal for preventing or treating Helicobacter pyroli infection, is new, where:

(a) the first polypeptide comprises a sequence identical or similar to, residues 21-270 of a 270 amino acid sequence, residues 24-273 of either of two 273 amino acid sequences, or residues 1-250 of a 277 amino acid sequence, all fully defined in the specification; and

(b) the second polypeptide comprises a sequence identical or similar to, residues 28-260 of a 260 amino acid sequence, residues 28-260 of either of two 260 amino acid sequences, residues 1-233 of a 268 amino acid sequence, or residues 53-97 of a 97 amino acid sequence, all fully defined in the specification.

INDEPENDENT CLAIMS are also included for the following:

(1) a fusion polypeptide for use in preventing or treating Helicobacter pyroli infection, comprising the two amino acid sequences of the novelty;

(2) a vaccine comprising the fusion polypeptide of (1) and a mucosal adjuvant and/or delivery system.

(3) a nucleic acid encoding the fusion polypeptide of (1), and comprising:

(a) a first nucleotide sequence identical or similar to, residues 61-777 of an 813 nucleotide sequence, residues 70-786 of either of two 822 nucleotide sequences, and nucleotides 82-798 of an 831 nucleotide sequence, all fully defined in the specification; and

(b) a second nucleotide sequence identical or similar to residues 873-1572 of a 1670 nucleotide sequence, residues 873-1572 of a 1670 nucleotide sequence; residues 82-783 of a 783 nucleotide sequence, residues 106-804 of an 804 nucleotide sequence, and residues 157-294 of a 294 nucleotide sequence.

ACTIVITY - Antibacterial.

Groups of mice were immunized intranasally with (A) purified recombinant HpaA (182 micro-g), (B) purified recombinant HOP38 (182 micro-g), (C) both HpaA and HOP38 (91 micro-g of each), (D) Helicobacter pylori whole cell lysate (100 micro-g), or (E) buffer. Immunizations were performed in the presence of CT adjuvant (10 micro-g). For HpaA, a polypeptide comprising residues 20-260 of a 260 amino acid sequence, fully defined in the specification, but with threonine at position 223 instead of alanine, was used. For HOP38, a polypeptide comprising residues 24-262 of a 273 amino acid sequence, fully defined in the specification, was used. Treatment of pre-existing

H . pylori infection was assessed by quantitative urease 2 weeks after experimental challenge with 10 to the power 6 colony forming units of H . pylori SSI by gavage. Mice were immunized at weekly intervals for 4 weeks. Half the total volume of the formulation was administered into each nostril. Two weeks after the last immunization, mice were sacrificed and stomach tissue harvested for quantitative urease assay. Results for the extent of H . pylori infection (by urease assay) were, for (A) 2.91E+04 +/-19624; (B) 3.87E+04 +/-35590; (C) 6.43E+03 +/-5495; (D) 3.40+03 +/-1838; and (E) 7.87E+04 +/-60473.

MECHANISM OF ACTION - Synergist; vaccine.

USE - For preventing or treating Helicobacter pylori infection.

pp; 65 DwgNo 0/0

6/AB/53 (Item 2 from file: 351)
DIALOG(R)File 351:Derwent WPI

012999349
WPI Acc No: 2000-171201/200015
XRAM Acc No: C00-053281

Use of Lactobacillus-derived urease , as a vaccine for preventing or treating Helicobacter infection and conditions including gastric ulcer , gastritis and gastric cancer caused by the infection

Patent Assignee: CHEIL JEDANG CORP (CHEI-N)
Inventor: PARK J B
Number of Countries: 081 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 200003730	A1	20000127	WO 98KR216	A	19980716	200015	B
AU 9884643	A	20000207	AU 9884643	A	19980716	200029	
			WO 98KR216	A	19980716		

Priority Applications (No Type Date): WO 98KR216 A 19980716
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 200003730	A1	E	38	A61K-039/07	

Designated States (National): AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW

Designated States (Regional): AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW

AU 9884643	A		A61K-039/07	Based on patent WO 200003730

Abstract (Basic): WO 200003730 A1
Abstract (Basic):

NOVELTY - A vaccine for generating protective immunity against Helicobacter (Hb) infection in a mammalian host comprises a polyaminoacid preparation including epitopes exhibited by a Lactobacillus (Lb)-derived urease in combination with a carrier or diluent.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a vaccine for inducing a passively protective potency against Hb infection in mammals comprising Lb-derived urease-specific IgA antibody to the passive protective potency with a carrier, the antibody being produced from a mammalian host immunized with the urease which is able to produce a protective immune response against Hb infection;

(2) a process for assaying protective response in a mammal infected with Hb organism comprising determining the presence of antibody

reactive with epitopes exhibited by (Lb)-derived urease endogenous to the Hb organism within a sample collected from a gastric biopsy of the mammal.

ACTIVITY - Antibacterial; Antiulcer; Antiinflammatory; Cytostatic.

MECHANISM OF ACTION - Vaccine . Lactobacillus fermentum (LF) ATCC 11739 was cultured and urease fractions were isolated. Mice were orally immunized with 30micro-g of purified LF urease coupled to 1mg of hydroxyapatite plus 10micro-g of cholera toxin adjuvant at day 0, 7, 14, and 21. At day 28, 30 and 32, mice were challenged with 108 H . felis (HF). For comparison purpose, similar SPF BALB/c mice were orally immunized with whole LF lysate (sonicate) and 10micro-g of cholera toxin at day 0, 7, 14 and 21. To evaluate the protection against HF colonization, gastric biopsies from each animal were screened for the presence of HF by assessing urease activity by the CLO test. The results showed that the oral immunization of mice with LF urease affords a statistically significant protection, compared to the immunization of mice with LF sonicate or cholera toxin. 7 of 10 mice immunized with LF sonicate and the 10 mice immunized with cholera toxin were infected with HF, only 4 of 10 mice immunized with LF urease were infected with HF. 30% of the mice immunized with LF sonicate and challenged with HF were protected and all of the mice immunized with cholera toxin and challenged with HF were not protected, 60% of the mice immunized with LF urease were protected from HF challenge.

USE - The vaccines are used for the prevention and treatment of Hb infection in mammals. They can be used for treating or preventing gastric ulcer , gastric ulcer , gastritis , gastric cancer, and other conditions which arise as a result of the presence of H. pylori and/or H. heilmanii.

pp; 38 DwgNo 0/2

6/AB/54 (Item 3 from file: 351)
DIALOG(R)File 351:Derwent WPI

011008950
WPI Acc No: 1996-505900/199650
Related WPI Acc No: 1995-006797; 1995-200383
XRAM Acc No: C96-158680

New immunogenic compsn. contg. UreB and HspA antigens of Helicobacter - for treatment and prevention of esp. H pylori infection, also new antibodies specific for these antigens.

Patent Assignee: INST NAT SANTE & RECH MEDICALE (INRM); INST PASTEUR (INSP)
Inventor: FERRERO R L; LABIGNE A; SUERBAUM S; THIBERGE J
Number of Countries: 070 Number of Patents: 002
Patent Family:

Patent No	Kind	Date	Applicat No	Kind	Date	Week	
WO 9634624	A1	19961107	WO 96EP1834	A	19960502	199650	B
AU 9656934	A	19961121	AU 9656934	A	19960502	199711	

Priority Applications (No Type Date): US 95447177 A 19950519; US 95432697 A 19950519
Patent Details:

Patent No	Kind	Lan	Pg	Main IPC	Filing Notes
WO 9634624	A1	E	184	A61K-039/106	

Designated States (National): AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
Designated States (Regional): AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG

AU 9656934 A A61K-039/106 Based on patent WO 9634624

Abstract (Basic): WO 9634624 A

A compsn. (A) comprises a mixture of Helicobacter antigens consisting essentially of UreB and HspA of H. pylori, or peptides with at least 75, pref. 80-90% similarity with them, or their fragments able to elicit antibodies recognised by H. pylori or a cellular response against H. pylori infection. Also new are antibodies (Ab), poly- or mono-clonal, directed against (A).

USE - (A) is useful as a vaccine to protect humans or other animals (esp. cats and dogs) against Helicobacter infection or as therapeutic agents to treat such infections. Partic. they are used to provoke a mucosal response, esp. practically the same response as provided by a total cell extract of the pathogen. Ab can also be used to prevent or treat infections, partic. by H.pylori of H. felis.

ADVANTAGE - (A) is the first recombinant subunit vaccine to induce an immunoprotective response against gastric Helicobacter infection. HspA acts as a chaperonin that increases urease activity and it also enhances protection.

Dwg.0/20

6/AB/55 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0256119 DBA Accession No.: 2000-10609 PATENT
Method for producing anti-pylorospirobacillus immune eggs - by injecting pyloric helicobacterium urease gene into fowl for vaccine production
AUTHOR: Chen H
CORPORATE SOURCE: People's Republic of China.
PATENT ASSIGNEE: Chinese-Acad.Sci. 2000
PATENT NUMBER: CN 1245011 PATENT DATE: 20000223 WPI ACCESSION NO.: 2000-388171 (2034)
PRIORITY APPLIC. NO.: CN 98117332 APPLIC. DATE: 19980817
NATIONAL APPLIC. NO.: CN 98117332 APPLIC. DATE: 19980817
LANGUAGE: CN
ABSTRACT: A method for producing anti-pyloric helicobacterium immune eggs of fowls, which can be used to cure active gastritis and peptic gastric ulcer as it can suppress the activity and reproduction of pyloric helicobacterium urease (EC-3.5.1.5) is new and involves separating and purifying the expressed product containing pyloric helicobacterium urease gene UreA or UreB in colibacillus to obtain alpha-subunit and beta-subunit of pyloric helicobacterium urease , respectively diluting with buffering liquid of potassium phosphate, adding isovolume F's complete assistant, ultrasonic stirring and injecting it into musculti thoraci of laying fowls. The fowls will lay out said anti-pyloric helicobacterium immuno eggs, whose yolk can be eaten for an immune purpose.

6/AB/56 (Item 2 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0250890 DBA Accession No.: 2000-05380 PATENT
Use of Lactobacillus-derived urease , as a vaccine for preventing or treating Helicobacter infection and conditions including gastric ulcer , gastritis and gastric cancer caused by the infection - Lactobacillus fermentum culture for urease production and enzyme or enzyme plus cholera toxin fusion protein application in vaccine

AUTHOR: Park J B
CORPORATE SOURCE: Seoul, Korea.
PATENT ASSIGNEE: Cheil-Jedang 2000
PATENT NUMBER: WO 200003730 PATENT DATE: 20000127 WPI ACCESSION NO.: 2000-171201 (2015)
PRIORITY APPLIC. NO.: WO 98KR00216 APPLIC. DATE: 19980716
NATIONAL APPLIC. NO.: WO 98KR216 APPLIC. DATE: 19980716
LANGUAGE: English
ABSTRACT: A vaccine for generating protective immunity against Helicobacter infection in a mammalian host comprises a polyamino acid preparation including epitopes exhibited by a Lactobacillus-derived urease (EC-3.5.1.5) in combination with a diluent or adjuvant. Also claimed are: a vaccine for inducing passive protection against Helicobacter infection in mammal comprising Lactobacillus-derived urease -specific IgA antibody (or anti-idiotype antibody) to the passive protective potency with the adjuvant, the antibody being produced from a mammal host immunized with the urease which is able to produce a protective immune response against Helicobacter infection; and a method for assaying protective response in a mammal infected with Helicobacter sp. involving determining the presence of antibody reactive with epitopes exhibited by Lactobacillus-derived urease endogenous to the Helicobacter organism within a sample collected from a gastric biopsy of the mammal. Lactobacillus fermentum ATCC 11739 or Lactobacillus reuteri can be cultured for urease production and the enzyme may be used alone or as a fusion protein with e.g. cholera toxin in vaccine production. (38pp)

6/AB/57 (Item 3 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0205065 DBA Accession No.: 97-00186 PATENT
Vaccine for inducing mucosal response to Helicobacter containing multimeric urease - Helicobacter pylori recombinant urease production by plasmid pORV214 expression in Escherichia coli, for application as a recombinant vaccine
AUTHOR: Lee C K; Monath T P; Ackerman S K; Thomas Jr W D; Soman G; Kleanthous H; Weltzin R A; Pappo J; Ermak T; Guirakhoo F; Bhagat H; Sussman I
CORPORATE SOURCE: Cambridge, MA, USA.
PATENT ASSIGNEE: Oravax 1996
PATENT NUMBER: WO 9633732 PATENT DATE: 961031 WPI ACCESSION NO.: 96-497373 (9649)
PRIORITY APPLIC. NO.: US 568122 APPLIC. DATE: 951206
NATIONAL APPLIC. NO.: WO 96US5800 APPLIC. DATE: 960425
LANGUAGE: English
ABSTRACT: A vaccine for inducing a mucosal immune response to Helicobacter comprises, apart from carrier or diluent, multimeric complexes (A) of recombinant, enzymatically inactive Helicobacter urease (EC-3.5.1.5). Also new are a composition for treating gastroduodenal infections containing antigen from the pathogen, and at least one antibiotic, antisecretory, and Bi salt. The vaccines are used to treat or prevent Helicobacter sp., especially Helicobacter pylori infections, and induce a protective, secretory IgA response. A 2.5 kb fragment containing both ureA and ureB gene of H . pylori CPM360 was isolated by the polymerase chain reaction and cloned into plasmid pET24 to form plasmid pORV214. This was used to transform Escherichia coli BL21-DE3. The transformants were cultured, lysed and soluble urease was recovered from the supernatant. Size-exclusion chromatography of the product showed it to exist mainly as the hexamer

(over 70%) and octomer (5-20%). It had no enzymatic activity. (98pp)

6/AB/58 (Item 4 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0192476 DBA Accession No.: 96-02669 PATENT
Vaccine and therapeutic composition containing Helicobacter pylori HAP protein - recombinant vaccine production
AUTHOR: Dettmar P W; Smith A W
CORPORATE SOURCE: London, UK.
PATENT ASSIGNEE: Reckitt 1996
PATENT NUMBER: DE 19523554 PATENT DATE: 960104 WPI ACCESSION NO.: 96-050293 (9606)
PRIORITY APPLIC. NO.: GB 9413073 APPLIC. DATE: 940629
NATIONAL APPLIC. NO.: DE 4023554 APPLIC. DATE: 950628
LANGUAGE: German
ABSTRACT: A vaccine or therapeutic composition contains Helicobacter pylori HAP (hemagglutinin/protease) protein, or a fragment of it. Also disclosed is a 1460 bp DNA sequence and a 256 amino acid protein sequence encoding HAP. HAP, or its fragments, can be a recombinant protein or polypeptide, and preferably fragments contain the zinc-binding region or the protease active site. Compositions may contain 2 or more HAP-related components, optionally also other antigenic compounds from other sources, e.g. from H . pylori cytotoxin, heat-shock protein or urease , or cholera toxin subunits. Usual carriers and adjuvants can be included. HAP and its fragments can be made by usual methods of peptide synthesis or by recombinant DNA methods. The compositions are used to treat or prevent infection by H . pylori which is implicated in gastric and duodenal ulcers and stomach cancer. (6pp)

6/AB/59 (Item 5 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0188790 DBA Accession No.: 95-13795 PATENT
Composition for treating Helicobacter infection - Helicobacter pylori recombinant urease monoclonal antibody administered using e.g. Salmonella typhimurium, Bacillus sp., yeast or herpes virus vector, for gastroduodenal disease therapy
AUTHOR: Michetti P; Corthesy-Theulaz I; Blum A; Davin C; Haas R; Kraehen-Buhl J P; Saraga E
PATENT ASSIGNEE: Oravax 1995
PATENT NUMBER: WO 9522987 PATENT DATE: 950831 WPI ACCESSION NO.: 95-320292 (9541)
PRIORITY APPLIC. NO.: US 200346 APPLIC. DATE: 940223
NATIONAL APPLIC. NO.: WO 95US2202 APPLIC. DATE: 950223
LANGUAGE: English
ABSTRACT: The following are claimed: (1) the use of a composition, containing Helicobacter sp. urease (EC-3.5.1.5) peptide (I), in the production of a medicament for the treatment of a gastroduodenal disease in a mammal; (2) the use of a monoclonal antibody which recognizes Helicobacter urease ; and (3) compositions containing the ureB subunit of Helicobacter pylori urease , a mucosal adjuvant and hydroxyapatite, and containing the ureB subunit in the form of a fusion protein which is genetically linked to the cholera toxin B subunit. Preferably, the composition is contained in a recombinant live vector, or a recombinant carrier system which expresses Helicobacter urease

. The live vector is selected from Salmonella typhimurium, Salmonella typhi, Shigella sp., Bacillus sp., Lactobacillus sp., Mycobacterium bovis BCG, Escherichia coli, Vibrio cholerae, Campylobacter sp., yeast, herpes virus, adeno virus, polio virus, vaccinia virus and avipox virus. The recombinant carrier system is selected from bluetongue virus-like particles, rota virus-like particles and Ty particles. (114pp)

6/AB/60 (Item 6 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0183308 DBA Accession No.: 95-10129
Identification of a novel protective antigen in Helicobacter felis - using a monoclonal antibody panel, for potential use in vaccine development (conference abstract)
AUTHOR: Blanchard T G; Nedrud J G; Czinn S J
CORPORATE AFFILIATE: Univ.Case-Western-Reserve-Inst.Pathol.
CORPORATE SOURCE: Institute of Pathology, Case Western Reserve University, Cleveland, OH 44106-4943, USA.
JOURNAL: Gut (37, Suppl.1, A31) 1995
ISSN: 0017-5749 CODEN: GUTTAK
CONFERENCE PROCEEDINGS: European Helicobacter pylori Study Group, VIIIth International Workshop on Gastro-duodenal Pathology and Helicobacter pylori, Edinburgh, Scotland, 7-9 July, 1995.
LANGUAGE: English
ABSTRACT: A panel of 9 Helicobacter felis-specific monoclonal antibodies (MAb) was used to identify protective antigens via a passive neutralization experiment which tested for their capacity to protect mice from colonization with the bacterium. Each MAb was incubated with 1 million H . felis prior to oral inoculation of mice. One of the MAbs, IgG-50, prevented colonization in 6/7 (86%) inoculated animals as determined by a positive urease (EC-3.5.1.5) reaction by gastric biopsies 1 wk after inoculation. Immunoprecipitation of an H . felis protein preparation demonstrated that IgG-50 was specific for a protein of approximately 13 kD. This protein was found to bind nickel using metal chelate chromatography, a characteristic associated with the H . pylori heat shock protein-A. However, amino acid analysis of this protein indicated that it was probably distinct from the heat shock protein-A. These data suggest that a low molecular weight protein other than urease may serve as a potential vaccine candidate for Helicobacter immunizations. (0 ref)

6/AB/61 (Item 7 from file: 357)
DIALOG(R)File 357:Derwent Biotech Res.

0180821 DBA Accession No.: 95-08841 PATENT
Oral vaccines against Helicobacter infections - containing inactivated urease or urease-containing bacterium
AUTHOR: LeVeen H H; Laveen E G; Laveen R F
PATENT ASSIGNEE: LeVeen H H 1995
PATENT NUMBER: EP 654273 PATENT DATE: 950524 WPI ACCESSION NO.: 95-187057 (9525)
PRIORITY APPLIC. NO.: US 185749 APPLIC. DATE: 940124
NATIONAL APPLIC. NO.: EP 94308551 APPLIC. DATE: 941118
LANGUAGE: English
ABSTRACT: Use of a non-enzymatic urease (EC-3.5.1.5) antigen for the production of a medicament for treating and/or preventing infections of

animals and humans caused by Helicobacter sp. (especially Helicobacter pylori) is claimed. The antigen is preferably an acid urease of bacterial origin (Lactobacillus fermentum TK 1214, Lactobacillus reuteri, Lactobacillus ruminis, Bacillus sp. TB-90, Streptococcus bovis, Streptococcus reuteri or Streptococcus salivarius) or plant (jack bean) origin. The antigen has its urease activity inactivated by covalent bonding to increase the mol.wt. and is preferably a glutaraldehyde or formaldehyde inactivated acid urease . Also claimed are: an oral vaccine containing the urease antigen; a composition containing the urease antigen, preferably encapsulated with a peptically resistant material; a vaccine comprising live or killed L. fermentum containing the inactive acid urease ; use of killed or live bacterium containing the inactivated urease for manufacture of a medicament for oral immunization to urease and inhibition of urea turnover. The antigen can be used in prevention of duodenum ulcers , etc. (12pp)

6/AB/62 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08210076 References: 0
TITLE: Vaccinating against Helicobacter pylori infections: Reality and perspectives
AUTHOR(S): Labigne A (REPRINT); Ferrero R; Galmiche JP
CORPORATE SOURCE: INST PASTEUR,INSERM, U389, UNITE PATHOGENIE BACTERIENNE MUQUEUSES, 25 RUE DOCTEUR ROUX/F-75724 PARIS 15//FRANCE/ (REPRINT)
PUBLICATION TYPE: BOOK
PUBLICATION: UPDATE GASTROENTEROLOGY 1996, 1996, P49-54
GENUINE ARTICLE#: BH18H
PUBLISHER: JOHN LIBBEY EUROTEXT, 127 AVE DE LA REPUBLIQUE, 92120 MONTROUGE, FRANCE
ISBN: 2-7420-0150-6
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The high prevalence of Helicobacter pylori infections, the severity of certain associated pathologies (duodenal ulcers , lymphoma , gastric carcinoma) and the predictable gradual emergence of resistance to the antibiotics currently used are factors that have encouraged the development of a vaccine approach to H . pylori infections. Studies to date have demonstrated that it is possible to protect animals (mice, ferrets, cats) against Helicobacter infection by immunisation via the oral- gastric route using crude extracts of bacterial antigens combined with an adjuvant known to stimulate a mucosal immune response. More recently, better defined H . pylori antigens such as the urease subunits, the HspA protein or the VacA cytotoxin, have been identified as possible components of a recombinant subunit vaccine . Progress achieved over the last few years in animal models leads us to expect that a prophylactic and/or therapeutic vaccine will be a reality in the first decade of the 21st century.
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